World Journal of Diabetes

Submit a Manuscript: https://www.f6publishing.com

World J Diabetes 2024 June 15; 15(6): 1122-1141

DOI: 10.4239/wjd.v15.i6.1122

ISSN 1948-9358 (online)

REVIEW

Vasorelaxant effects of biochemical constituents of various medicinal plants and their benefits in diabetes

Sadettin Demirel

Specialty type: Cardiac and cardiovascular systems

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's classification
Scientific Quality: Grade B, Grade B
Novelty: Grade B
Creativity or Innovation: Grade B
Scientific Significance: Grade A

P-Reviewer: He YF, China

Received: December 30, 2023
Revised: March 7, 2024
Accepted: May 6, 2024
Published online: June 15, 2024
Processing time: 163 Days and 21.6 Hours

Sadettin Demirel, Medicine School, Physiology Department, Bursa Uludag University, Bursa 16059, Türkiye

Corresponding author: Sadettin Demirel, BSc, MSc, PhD, Associate Professor, Medicine School, Physiology Department, Bursa Uludag University, Nilufer, Bursa 16059, Türkiye. sdemirel@uludag.edu.tr

Abstract

Endothelial function plays a pivotal role in cardiovascular health, and dysfunction in this context diminishes vasorelaxation concomitant with endothelial activity. The nitric oxide-cyclic guanosine monophosphate pathway, prostacyclin-cyclic adenosine monophosphate pathway, inhibition of phosphodiesterase, and the opening of potassium channels, coupled with the reduction of calcium levels in the cell, constitute critical mechanisms governing vasorelaxation. Cardiovascular disease stands as a significant contributor to morbidity and mortality among individuals with diabetes, with adults afflicted by diabetes exhibiting a heightened cardiovascular risk compared to their non-diabetic counterparts. A plethora of medicinal plants, characterized by potent pharmacological effects and minimal side effects, holds promise in addressing these concerns. In this review, we delineate various medicinal plants and their respective biochemical constituents, showcasing concurrent vasorelaxant and anti-diabetic activities.

Key Words: Medicinal plants; Vasorelaxation; Endothelium; Diabetes; Anti-diabetic

Core Tip: To the best of our knowledge, this study is pioneering, offering a unique perspective that addresses both vasorelaxation and diabetes concerning medicinal plants. The comprehensive collection of medicinal plant references presented in this study is anticipated to serve as a valuable resource, inspiring and guiding future investigations into cardiovascular diseases and diabetes.

Citation: Demirel S. Vasorelaxant effects of biochemical constituents of various medicinal plants and their benefits in diabetes. *World J Diabetes* 2024; 15(6): 1122-1141
URL: https://www.wjgnet.com/1948-9358/full/v15/i6/1122.htm
DOI: https://dx.doi.org/10.4239/wjd.v15.i6.1122

INTRODUCTION

Cardiovascular diseases (CVDs), stemming from disorders affecting the heart and blood vessels, claim tens of millions of lives globally every year[1]. The cardiovascular system comprises the heart and three distinct types of blood vessels[2]. The inner surface of blood vessels is constituted by endothelial cells referred to as the tunica intima layer[3]. Endothelial cells envelop the interior of the vessel and establish interaction with the blood[2]. These cells function as a barrier between the vessel lumen and wall, preventing blood clotting, while mediators released from them exert vasoactive effects[4]. Impaired endothelial function and diminished endothelium-associated vasorelaxation contribute to the development of various cardiovascular disorders, including hypertension and diabetes[5]. Concurrently, diabetic vasculopathy manifests as endothelial dysfunction, characterized by endothelial injury and vascular wall thickening[6].

Hemodynamic forces, such as shear stress, impact endothelial cells, causing unidirectional deformation of endothelial cells[7]. The equilibrium between vasodilator and vasoconstrictor agents regulates vascular tone. Endothelial dysfunction further results in elevated vascular tone, leading to cardiovascular disorders such as hypertension[8]. Vasodilatory agents like endothelium-derived hyperpolarizing factor, nitric oxide (NO), and prostacyclin (PGI_2) are produced by the endothelium in response to increased shear stress[9]. Various mechanisms, including the NO- cyclic guanosine monophosphate (cGMP) pathway, PGI_2-cyclic adenosine monophosphate (cAMP) pathway, phosphodiesterase (PDE) inhibition, and the opening of K^+ ion channels/reduction of intracellular Ca^{2+} levels, play crucial roles in vasorelaxation [10].

There are studies in the literature about the effects of medicinal plants on either vasorelaxation or diabetes. However, the absence of articles presenting the effects of medicinal plants on both vasorelaxation and diabetes necessitates the inclusion of this review in the literature. Addressing this gap will not only enhance our understanding but also aid in future studies on CVDs, as decreased vasorelaxation is a significant contributor to such conditions[11]. The mechanisms crucial for vasorelaxation are expounded upon in this review, along with accompanying figures. The review encompasses components and aspects of 85 medicinal plants, delineating their effects on vasorelaxation and diabetes in Table 1.

Several articles investigating the effects of plants on vasorelaxation are outlined below: Luna-Vázquez *et al*[12] identified 19 compounds isolated from 10 plants used in traditional Mexican medicine that can alter arterial smooth muscle tone. Guerrero *et al*[13] illustrated that different fractions obtained from two Latin American plants used in Amerindian traditional medicine possess vasorelaxation effects. Luna-Vázquez *et al*[14] elucidated the mechanism of action of 207 vasorelaxant metabolites. Capettini *et al*[15] discovered that xanthones derived from Brazilian medicinal plants exhibit vasorelaxant and antioxidant properties. Tang *et al*[16] highlighted traditional medicinal plants with the potential to prevent and treat hypertension, cardiovascular, and cerebrovascular diseases. Malekmohammad *et al*[17] reported on metabolites of medicinal plants that stimulate critical vasorelaxation mechanisms.

Additionally, numerous articles explore the effects of plants on diabetes: Kadir *et al*[18] documented an ethnobotanical survey on antidiabetic plants used in traditional Bangladeshi medicine. Salehi *et al*[19] identified numerous plants and their components effective against diabetes. Trojan-Rodrigues *et al*[20] identified plant species widely used in diabetes treatment in the state of Rio Grande do Sul in southern Brazil. Garima *et al*[21] conducted an ethnobotanical survey on anticancer and antidiabetic plants used by local tribes in Mizoram, Northeast India.

NO-CYCLIC GUANOSINE 3’, 5’-MONOPHOSPHATE GUANOSINE PATHWAY

Vascular smooth muscle cell (VSMC) is stimulated by NO that is produced in a catalyzed reaction, formed citrulline amino acid from arginine amino acid, by endothelial nitric oxide synthase (eNOS)[22]. The soluble guanylate cyclase receptor found in adjacent cells is activated by NO[23]. Thus, it is occurred to rise the level of cGMP, which forms vasodilation[10] (Figure 1).

PGI_2-CYCLIC ADENOSINE MONOPHOSPHATE PATHWAY

PGI_2, which activates the prostacyclin receptor included in the G protein-coupled receptor (GPCR), functions as a vasorelaxant factor[24]. The enzyme cyclooxygenase catalyzes arachidonic acid as a substrate, forming prostaglandin H_2, the precursor of PGI_2[25]. Additionally, prostacyclin synthase generates PGI_2, a lipid, when stimulated by various factors such as shear stress, cytokines, thrombin, and growth factors. The concentration of cAMP increases through the induction of adenylyl cyclase by PGI_2[25]. Consequently, this leads to a vasorelaxation impact on VSMCs[26] (Figure 2).

Table 1 Various medicinal plants with vasorelaxant activities and beneficial effects on diabetes

Plant	Vasorelaxation			Diabetes			[1]Ref.
	Component/extract	Part	Effect	Component/extract	Part	Effect	
Securigera securidaca L.	Hydroalcoholic extract	Seed	Endothelium-dependent vasorelaxation in hyper-cholesterolemic rats	Hydroalcoholic extract	Seed	Anti-diabetic	[61,62]
Parkia biglobosa	Aqueous extract	Seed	Smooth muscle vasorelaxation *via* endothelium due to PGs	Hydromethanolic extract	Stem bark	Anti-diabetic	[63,64]
Orthosiphon stamineus	Eupatorin	-	Endothelium-intact aortic ring vasore-laxation on contraction by KCl and endothelium-denuded aortic ring vasore-laxation on contraction by PE	Water extract, methanolic extract	Aerial parts	Anti-diabetic	[65,66]
Rosa damascena Mill.	2-phenyl ethyl alcohol	Spent flower	Vasorelaxation on rat aorta and mesenteric artery without vascular endothelium effect	Methanolic extract	Flower	α-glucosidase inhibitor	[67,68]
Eruca sativa Mill.	Crude extract, fractions	-	Endothelium-dependent vasorelaxation on aortic rings of normotensive rats and endothelium-independent vasorelaxation on aortic rings of hypertensive rats	Hexane fraction and its fatty acid-rich fraction	Leaf	Anti-diabetic	[69,70]
Echinodorus grandiflorus	Ethanolic extract and its butanol fraction	Leaf	Vasorelaxation on resistance vessels by releasing PGI_2 and NO through B_2-bradykininergic and endothelial M_3-muscarinic receptors and then activating K^+ channels in vascular smooth muscle	Ethanolic extract	Leaf	Antiglycation	[52,71]
Gynura procumbens	Aqueous extract, methanolic extract	Leaf	Vasorelaxation by activating muscarinic M_3 receptors in the existence of endothelium and vasorelaxation on rat thoracic aorta through cholinergic pathway	Leaf extract	Leaf	Anti-diabetic	[52,72]
Garcinia cowa	Leaf extract	Leaf	Vasorelaxation by activating K_{ATP} and generating prostanoids and NO	Compounds 4 and 8	Leaf	α-glucosidase inhibitor	[73,74]
Bauhinia forficata Link	Ethyl-acetate plus butanol fraction, kaempferitrin, kaempferol	Leaf	Vasorelaxation on the thoracic aorta of hypertensive and normotensive rats	Methanolic extract	Leaf, stem	Hypoglycemic	[39,75]
Nelumbo nucifera	Extracts of spornioderm	Spornioderm	Endothelium-dependent vasorelaxation by activating PI3K-eNOS-sGC pathway	Seed extract	Seed	Hypoglycemic	[76,77]
Cimicifuga racemosa	Black cohosh extract		Vasorelaxation by way of endothelium-dependent and -independent mechanisms on pre-contracted rat thoracic aortic rings by NE	Extract Ze 450		Decreasing plasma glucose in ob/ob mice with diabetes	[78,79]
Crocus sativus L.	Crocetin		Endothelium-dependent vasorelaxation through endothelial NO	Crocins	Stigma	Decreasing levels of glucose and increasing expression of insulin in zebrafish embryo	[80,81]

Morus alba	Root bark extract	Root bark	Endothelium-dependent vasorelaxation partially *via* NO-cGMP pathway containing TEA sensitive K^+ channels activation	Kuwanon H, morin, morusin, oxyresveratrol, kuwanon G	Root bark	α-glucosidase inhibitor	[46,82]
Erigeron breviscapus Hand Mazz.	Scutellarin		Endothelium-independent vasorelaxation on thoracic artery rings by blocking the influx of extracellular Ca^{2+} as independent from VDCCs	Scutellarin		Induces autophagy signal pathway by upregulating autophagy-related factors and blocks apoptotic signal pathway by downregulating apoptosis-related factors, and consequently relief of type 2 DC	[83,84]
Vernonia amygdalina	Ethanolic extract	Leaf	Vasorelaxation by upregulating NO/cGMP and PGI_2 signalization pathways and modulating muscarinic and β_2-adrenergic receptor levels, and Ca^{2+}/K^+ channels	Leaf extracts	Leaf	α-amylase inhibitor	[54,85]
Glycyrrhiza uralensis	50% ethanolic extract		Vasorelaxation in endothelium-intact aortic rings pre-contracted with PE and KCl	Glycyrrhiza flavonoids	Root	α-glucosidase inhibitor	[86,87]
Salvia miltiorrhiza	*S. miltiorrhiza* extract		Vasorelaxation of renal, mesenteric, and femoral arteries at low extract concentration and vasorelaxation of coronary arteries at all extract concentrations tested	*S. miltiorrhiza* extract	Root	Hypoglycemic	[88,89]
Sophora alopecuroides	Oxysophoridine		Vasorelaxation on thoracic aorta rings by being related to K_{ATP} and K_V channels	Aloperine	Aerial parts	Hypoglycemic	[90,91]
Coriandrum sativum	Coriander crude extract		Vasorelaxation on contracted rabbit aorta with PE and K^+ (80 mM)	Aqueous extract	Leaf, stem	α-glucosidase inhibitor	[53,92]
Ligusticum chuanxiong Hort.	Ethanolic extract	Rhizome	Induction of eNOS-derived NO production	Ethanolic extract	Rhizome	Amelioration of diabetic nephropathy	[58,93]
Sorbus commixta Hedl.	Methanolic extract	Cortex	Vasorelaxation on vascular smooth muscle through NO-cGMP pathway	Lupenone, lupeol	Stem bark	PTP1B inhibitor	[94,95]
Aronia melanocarpa	Conjugated cyanidins, chlorogenic acids	Juice	Inducing endothelial NO production in a coronary artery by getting eNOS phosphorylation due to redox-sensitive activation of the Src/PI3-kinase/Akt pathway		Juice	Hypoglycemic	[96,97]
Annona squamosa	Esquamosan	Leaf	Endothelium-independent vasorelaxation on isolated rat aorta *via* prevention of intracellular Ca^{2+} increasing by blocking VDCCs and intracellular storage channels in VSMCs	Hexane extract		Hypoglycemic	[98,99]
Artemisia herba alba	Aqueous extract		Vasorelaxation through endothelial NO production	Aqueous extract	Leaf or bark	Lowering blood glucose levels	[100,101]
Ajuga iva (L.) Schreber (Labiatae)	Aqueous extract		*In vitro*, NO-mediated and NO-independent vasorelaxation; *ex vivo*, endothelium-independent vasorelaxation	Lyophilized aqueous extract	Whole plant	Hypoglycemic	[102,103]

Mansoa hirsuta D.C.	Ethanolic extract	Leaf	Endothelium-dependent vasorelaxation	Fraction		α-amylase inhibitor	[104,105]
Mentha longifolia	N-butanol fraction	Aerial parts	Endothelium-independent relaxation owing to increase of cAMP and cGMP levels by blocking diverse PDEs			Anti-diabetic	[40,106]
Euphorbia humifusa Willd.	Total flavonoids of *E. humifusa*		Vasorelaxation on rat thoracic aorta with endothelium-dependent NO-cGMP signaling by inducing PI3K/Akt-and Ca^{2+}-eNOS-NO signaling pathway; relaxation of VSMCs by stimulating NO-sGC-cGMP-protein kinase G signaling *via* L-type Ca^{2+} channel activity inhibition	Vitexin and astragalin	Whole plant	Anti-diabetic	[42,107]
Sophora flavescens	Ethanolic extract	Root	Relaxation of vascular smooth muscle *via* the endothelium-dependent NO-sGC-cGMP signaling pathway	Four minor flavonoids (1-4)	Root	α-glucosidase inhibitor	[108,109]
Kaempferia parviflora	Ethanolic extract	Rhizome	Vasorelaxation in a dose-dependent manner on aortic rings pre-contracted with PE			Anti-diabetic	[19,110]
Angelica decursiva	70% ethanolic extract	Root	Endothelium-independent vasorelaxation *via* K_{ATP} channels as well as blocking of Ca^{2+} influx through VDCCs and ROCCs	Coumarins 1-6		α-glucosidase inhibitor, PTP1B inhibitor	[111,112]
Hintonia latiflora	*H. latiflora* extract, neoflavonoid coutareagenin	Bark	Vasorelaxation on aortic rings pre-contracted with NE	*H. latiflora* extract, neoflavonoid coutareagenin	Bark	Diminishing blood glucose	[113,114]
Kaempferia galanga L.	Ethyl-p-methoxycinnamate	Rhizome	Endothelium-independent but K^+ channel-dependent vasorelaxation	Novel *K. galanga* rhizome essential oil rich in ethyl p-methoxy cinnamate	Rhizome	Anti-diabetic	[115,116]
Prunus mume Sieb. et Zucc.	70% ethanolic extract	Bark	Endothelium-dependent vasorelaxation on isolated rat aortic rings through NO/sGC/cGMP and PGI_2 pathway; vasore-laxation partially *via* K_{Ca}, K_{ATP}, K_V, and K_{ir} channels	70% ethanolic extract	Leaf	Anti-diabetic	[116,117]
Bacopa monnieri	Saponins (bacoside A and bacopaside I), flavonoids (luteolin and apigenin)		Endothelium-intact vasorelaxation and endothelium-denuded vasorelaxation	Bacosine		Antihyperglycemic	[118,119]
Haloxylon scoparium	Aqueous extract		Vasorelaxation *via* Ca^{2+} channels blockade	Decoctate, methanolic extract, macerated methanol, ethyl; acetate extract	Aerial part	A-glucosidase inhibitor, a-amylase inhibitor, ß-asides inhibitor	[56,120]
Swietenia macrophylla King	50% ethanolic extract	Seed	Inhibiting IP_3R, blocking VOCC and activating K^+ channels; vasorelaxation *via* β_2-adrenergic pathway and NO/sGC/cGMP signaling pathways	Limonoids	Fruit	Anti-diabetic	[48,121]
Eucalyptus globulus	Aqueous extract	Leaf	Dose-dependent vasorelaxation on aortic rings by inducing NO production			Amelioration of hyperglycemia	[122,123]

Plumeria rubra	Aqueous-methanolic extract	Leaf	Concentration-dependent vasorelaxation on PE-induced spastic contractions and K^+ (80 mM)-induced spastic contractions	Compounds 1-4, 7, 8, and 16	Flower	α-glucosidase inhibitor, PTP1B inhibitor	[41,124]
Prunus persica	*P. persica* extract	Branch	Endothelium-dependent vasorelaxation *via* NO-sGC-cGMP, vascular PGI_2, and muscarinic receptor transduction pathways; vasorelaxation partially through K_{ATP}, BK_{Ca}, and K_V channels			Anti-diabetic	[19,125]
Prunus yedoensis Matsum.	Methanolic extract	Bark	Vasorelaxation due to activation of NO production through L-Arg and NO-cGMP pathways; vasorelaxation through blockade of extracellular Ca^{2+} channels	*P. yedoensis* extract	Leaf	Antihyperglycemic	[126,127]
Xanthoceras sorbifolia Bunge	Ethanolic extract	Leaf	Vasorelaxation on vascular smooth muscle through Akt- and SOCE-eNOS-sGC pathways		Wood	α-glucosidase inhibitor	[128,129]
Passiflora edulis	Hydroethanolic extract	Fruit peel	Vasorelaxation on mesenteric artery rings *via* activation of K^+ channels	Aqueous extract	Fruit peel	Anti-diabetic	[129,130]
Apium graveolens L.	Seed extract	Seed	Vasorelaxation through inhibition of ROCCs and VDCCs, the release of EDHF, and activation of K_v channels	Leaf extract	Leaf	Reducing pre-prandial blood glucose levels and post-prandial blood glucose levels in pre-diabetic elderly patients	[60,131]
Phyllanthus niruri L.	Methyl brevifolincarboxylate	Leaf	Inhibition of NE-induced vasoconstriction *via* ROCCs partially mediated by $(Ca^{2+})_i$ decrease	Aqueous extract, ethanolic extract	Aerial part	α-glucosidase inhibitor	[132,133]
Marrubium vulgare	Crude extracts	Aerial part	Inhibiting KCl-induced contraction on the rat aorta	Aqueous extract		Anti-diabetic	[134,135]
Psoralea corylifolia L.	*P. corylifolia* extract, bakuchiol, isobavachalcone, isopsoralen, psoralen	Seed	Endothelium-dependent vasorelaxation through NO-cGMP pathway; attenuating PE-induced vasoconstriction by inhibiting TRPC3 channels in a dose-dependent manner	Compounds 1, 2, 3, 6, 8	Seed	DGAT1 inhibitor, α-glucosidase inhibitor	[57,136]
Ginkgo biloba	Terpenoids (bilobalide, ginkgolides A, B, and C) and flavonoids (quercetin and rutin)		Concentration-dependent vasorelaxation	*G. biloba* extract		Antihyperglycemic	[137,138]
Rubus chingii	Ethanolic extract	Dried fruit	Vasorelaxation *via* Ca^{2+}-eNOS-NO signaling in endothelial cells and later NO-sGC-cGMP-K_V channel signaling in VSMCs	Ursane-type triterpenes	Fruit	PTP1B inhibitor	[55,139]
Bidens pilosa	Neutral extract	Leaf	Vasorelaxation and behaving as a Ca^{2+} antagonist	*B. pilosa* formulation		Anti-diabetic	[140,141]
Allium sativum	L-arginine in aged garlic extract		Endothelium-dependent vasorelaxation on the aorta by inducing NO formation	Silver nanoparticles	Bulb	Anti-diabetic	[142,143]
Petroselinum crispum	Aqueous extract	Aerial part	Vasorelaxation *via* VOCCs and ROCCs	*P. crispum* extract	Leaf	Decreasing blood glucose	[144,145]

Curcuma longa	Curcubisabolanin A	Rhizome	Partially endothelium-dependent vasorelaxation by regulating NO production in vascular endothelial cells *via* the PI3K/Akt/eNOS signaling pathway			Enhancing postprandial serum insulin levels with ingestion of 6 g of *C. longa*	[146,147]
Allium cepa	*A. cepa* peel hydroalcoholic extract	Peel	Decreasing aortic contractions probably through depression of Ca^{2+} influx from extracellular to intracellular, without including endothelium, NO, cGMP, and PGs			Diminishing blood glucose	[148,149]
Alpinia zerumbet	Essential oil	Leaf	Vasorelaxation by inhibiting both Ca^{2+} influx and Ca^{2+} release from intracellular storage; vasorelaxant effect *via* NOS/sGC pathway	Labdadiene	Rhizome	Antiglycation	[43,150]
Paeonia suffruticosa Andr.	1,2,3,4,6-penta-O-galloyl-beta-d-glucose	Root cortex	Concentration-dependent vasorelaxation on rat aorta pre-contracted with PE	Extract of moutan cortex	Root	Improving inflammation in AGEs-induced mesangial cell dysfunction and high-glucose-fat diet and STZ-induced DN rats	[151,152]
Nigella sativa	Seed extract	Seed	Endothelium-independent vasorelaxation on contraction stimulated by PE and KCl *via* inhibition of extracellular Ca^{2+} influx, K_{ATP} channels, and IP_3-mediated receptors	Crude aqueous extract	Seed	*In vitro*, suppressing electrogenic intestinal absorption of glucose directly; *in vivo*, ameliorating both body weight and glucose tolerance after chronic oral administration in rats	[153,154]
Myrciaria cauliflora Berg	Hydroalcoholic extract	Fruit peel	Endothelium-dependent vasorelaxation *via* NO/sGC/cGMP pathway	*M. cauliflora* extract	Lyophilized fruit	Hypoglycemic	[155,156]
Morus bombycis Koidzumi	100% ethanolic extract	Root bark	Vasorelaxation on isolated rat aortic preparations	2,5-dihydroxy-4,3-di(beta-D-glucopyranosyloxy)-trans-stilbene	Root	Hypoglycemic	[157,158]
Humulus lupulus L.	Aqueous hop extract		Vasorelaxation through NOS activation, COX products, and Ca^{2+} pathways in both male and female rats	Xanthohumol		α-glucosidase inhibitor	[159]
Sesamum indicum L.	Petroleum ether soluble fraction of root extract	Root	Endothelium-dependent vasorelaxation			Decreasing fasting blood sugar	[160,161]
Hibiscus sabdariffa	Hibiscus acid		Vasorelaxation by depression of intracellular Ca^{2+} influx through VDCCs	Ethyl acetate extract, ethanolic extract, aqueous extract	Flower	Anti-diabetic	[162,163]
Jasminum sambac	Hydroalcoholic leaf extract	Leaf	Vasorelaxation completely on endothelium-intact rabbit aorta contracted with PE; vasorelaxation partially on endothelium-intact rabbit aorta contracted with NE	Polyphenol extract	Leaf	Preventing and having a therapeutic effect on DC	[59,164]
Hancornia speciosa Gomes	Ethanolic extract	Leaf	NO- and endothelium-dependent vasorelaxation on rat aortic preparations through PI3K activation	Aqueous extract	Latex	Hypoglycemic	[165,166]
Pseuderanthemum	Water extract	Leaf	Vasorelaxation *via* partially vascular	80% ethanolic leaf extract	Leaf	Hypoglycemic	[167,168]

palatiferum			endothelium not with NO production and muscarinic receptor activation				
Terminalia superba	Methylene chloride extract, methylene chloride-methanol extract	Stem bark	Vasorelaxation partially *via* depression of extracellular Ca^{2+} influx and/or suppression of intracellular Ca^{2+} releasing in VSMCs; vasorelaxation *via* endothelial NO	Methylene chloride-methanol extract	Leaf	Anti-diabetic	[49,169]
Guazuma ulmifolia	Procyanidin fraction	Bark	Vasorelaxation through endothelium-related factors, including NO	Aqueous extract		Anti-diabetic	[170,171]
Persea americana Mill.	Aqueous leaf extract	Leaf	Vasorelaxation through endothelial NO production and releasing	Hydroalcoholic extract	Leaf	Anti-diabetic	[172,173]
Capparis aphylla	Crude extract	Aerial part	Endothelium-dependent vasorelaxation partially *via* atropine-sensitive NO pathway; endothelium-independent vasorelaxation partially *via* the Ca^{2+} channel blocking activity	Methanolic extract, active fraction	Stem	Decreasing blood glucose levels	[174,175]
Rheum undulatum	Piceatannol in rhizome extract	Rhizome	Vasorelaxation through endothelium-dependent NO signaling pathway	E-viniferin, piceatannol, and δ-viniferin in methanolic extract	Rhizome	PTP1B inhibitor	[176,177]
Globularia alypum	*G. alypum* extract		Vasorelaxation due to EDHF *via* endothelial muscarinic receptor activation	Methanolic extract, water extract	Leaf	Reducing fasting blood glucose	[178,179]
Gmelina arborea	Hexane extract	Leaf	Concentration-dependent vasorelaxation on isolated rat aorta	Aqueous extract	Bark	Antihyperglycemic	[50,180]
Coscinium fenestratum	*C. fenestratum* extract		Endothelium-dependent and -independent vasorelaxation on isolated aortic rings precontracted with PE and KCl	Alcoholic stem extract	Stem	Anti-diabetic	[181,182]
Myrtus communis L.	Crude methanolic extract	Aerial part	Vasorelaxation on isolated rabbit aorta preparations contracted with PE and K^{+}	Volatile oil		Hypoglycaemic	[183,184]
Thymus linearis Benth.	N-butanolic fraction	Aerial part	Endothelium-independent vasorelaxation due to increase in cAMP and cGMP *via* inhibition of several PDEs	Ethyl acetate extract, combined extract	Aerial part	A-amylase inhibitor	[185,186]
Vitex agnus-castus	*V. agnus-castus* extract	Fruit	Endothelium-dependent vasorelaxation *via* NO/cGMP and PGs production in the aorta	Hydroalcoholic extract	Desiccated fruit	Hypoglycemic	[51,187]
Anogeissus leiocarpus	Aqueous extract	Trunk bark	Endothelium-dependent NO-mediated vasorelaxation on porcine coronary arteries *via* redox-sensitive Src/PI3-kinase/Akt pathway-dependent activation of eNOS	Supernatant fraction, total extract	Root	Anti-diabetic	[188,189]
Zanthoxylum armatum DC	Tambulin in methanolic extract	Fruit	Influencing directly vascular smooth muscle through cAMP and/or cGMP-related relaxing pathways	Fruit, bark, and leaf extracts	Fruit, bark, and leaf	Anti-diabetic	[190,191]
Cymbopogon martinii	Crude methanolic extract	Leaf	Partial vasorelaxation on isolated rabbit aortic preparations contracted with PE and			A-glucosidase inhibitor	[192,193]

			K^+				
Moringa oleifera	*M. oleifera* leaf extract	Leaf	Endothelium-dependent vasorelaxation through EDHF-mediated hyperpolarization; endothelium-independent vasorelaxation due to inhibition of extracellular Ca^{2+} influx through VOCCs and ROCCs and suppression of sarcolemmal Ca^{2+} releasing through IP_3R Ca^{2+} channels	Methanolic extract	Pods	Anti-diabetic	[194,195]
Dalbergia odorifera T. Chen	Butein		Vasorelaxation on rat aorta; the novel cAMP-specific PDE inhibitor; vasorelaxant action related intact endothelium	Compounds in ethyl acetate soluble fraction	Heartwood	α-glucosidase inhibitor	[196,197]
Coptis chinensis	Berberine		Decreasing expression of miR-133a; enhancing BH4 levels and production of NO	Polysaccharide		Anti-diabetic	[38,198]
Angelica keiskei	Xanthoangelol, 4-hydroxyderricin, xanthoangelol E and F in EtOAc-soluble fraction, xanthoangelol B in EtOAc-soluble fraction	Root	Blocking PE-induced vasoconstriction through EDRF/NO synthesis and/or attenuation of PE-induced $(Ca^{2+})_i$ increase; blocking PE-induced vasoconstriction by reducing $(Ca^{2+})_i$ increase and directly inhibiting smooth muscle contraction	Flavonoid-rich ethanolic extract	Leaf	Hypoglycemia	[199,200]
Scutellaria baicalensis Georgi	Baicalin		Vasorelaxation on the mesenteric artery by stimulating BK_{Ca} channels and blocking VDCCs with endothelium-independent mechanisms, moreover by inducing cGMP/PKG and cAMP/PKA pathways	Root polysaccharide	Root	α-amylase inhibitor, α-glucosidase inhibitor	[201,202]
Ocimum gratissimum	Essential oil		Dose-dependent vasorelaxation on resistance blood vessels of rat mesenteric vascular beds completely *via* NO; dose-dependent vasorelaxation on rat aorta partially mediated by NO	Chicoric acid in leaf extract	Leaf	Hypoglycemic	[203,204]

[1]The first reference is associated with vasorelaxation and the second with diabetes.

ACh: Acetycholine; AGEs: Advanced glycation end-products; BH4: Tetrahydrobipterin; BK_{Ca} channel: Large-conductance Ca^{2+}-activated K^+ channel; COX: Cyclooxygenase; DGAT1 inhibitor: Diacylglycerol acyltransferase-1 inhibitor; DC: Diabetic cardiomyopathy; DN: Diabetic nephropathy; eNOS: Endothelial nitric oxide synthase; EDHF: Endothelium-derived hyperpolarizing factor; EDRF: Endothelium-derived relaxing factor; EtOAc: Ethyl acetate; IP_3R: Inositol triphosphate receptor; K_{ATP} channel: ATP-sensitive K^+ channel; K_{Ca} channel: Ca^{2+} activated K^+ channel; K_{ir} channel: Inward rectifier-type K^+ channel; K_v channel: Voltage-sensitive K^+ channel; NO: Nitric oxide; NE: Norepinephrine; PDE: Phosphodiesterase; PE: Phenylephrine; PG: Prostaglandin; PGI_2: Prostacyclin; PI3K: Phosphatidyl-inositol 3-kinase; PKA: Protein kinase A; PKG: Protein kinase G; PTP1B inhibitor: Protein tyrosine phosphatase 1B inhibitor; ROCC: Receptor-operated Ca^{2+} channel; sGC: Soluble guanylate cyclase; SOCE: Store-operated Ca^{2+} entry; STZ: Streptozotocin; TEA: Tetraethylammonium; TRPC3 channel: Transient receptor potential canonical 3 channel; VDCC: Voltage-dependent Ca^{2+} channel; VOCC: Voltage-operated Ca^{2+} channel; VSMC: Vascular smooth muscle cell.

PDE INHIBITION

cGMP and cAMP, serving as second messengers in the cell, are hydrolyzed by cyclic nucleotide PDEs[27]. In this manner, PDE enzymes facilitate the breakdown of cAMP into 5′-AMP and cGMP into 5′-GMP. Preventing PDE activation results in heightened concentrations of cyclic nucleotides, such as cAMP and cGMP, promoting vasorelaxation[28] (Figure 3).

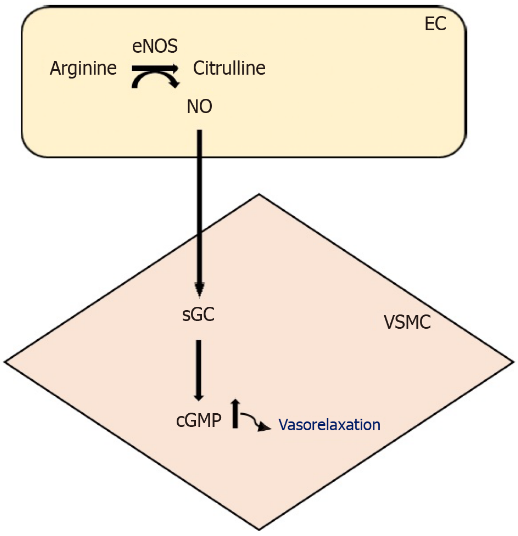

Figure 1 Vasorelaxation effect of nitric oxide-cyclic guanosine monophosphate pathway. cGMP: Cyclic guanosine monophosphate; EC: Endothelial cell; eNOS: Endothelial nitric oxide synthase; NO: Nitric oxide; sGC: Soluble guanylate cyclase; VSMC: Vascular smooth muscle cell.

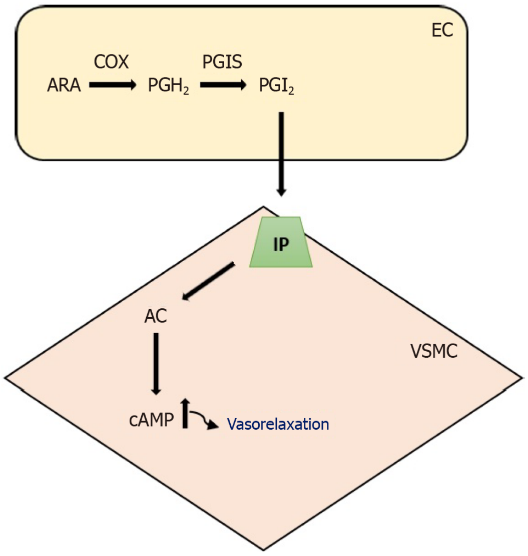

Figure 2 Vasorelaxation effect of PGI_2-cyclic adenosine monophosphate pathway. AC: Adenylyl cyclase; ARA: Arachidonic acid; cAMP: Cyclic adenosine monophosphate; COX: Cyclooxygenase; EC: Endothelial cell; PGI_2: Prostacyclin; IP: Prostacyclin receptor; PGIS: Prostacyclin synthase; PGH_2: Prostaglandin H_2; VSMC: Vascular smooth muscle cell.

OPENING K^+ ION CHANNELS AND REDUCING CA^{2+} LEVELS IN CELLS

VSMCs harbor different K^+ channels, including voltage-sensitive K^+ (K_V) channels, inward rectifier-type K^+ (K_{ir}) channels, ATP-sensitive K^+ (K_{ATP}) channels, and Ca^{2+}-activated K^+ (K_{Ca}) channels[29]. Activation of K^+ channels induces membrane hyperpolarization, leading to the cessation of voltage-dependent Ca^{2+} channels' (VDCCs) activity, blocking the entry of Ca^{2+} into the cell, and ultimately resulting in vasorelaxation[30]. Additionally, the relaxation of VSMCs occurs when receptor-operated Ca^{2+} channels or VDCCs, responsible for intracellular calcium ion procurement, are blocked[31].

Diabetes mellitus (DM), a metabolic disease, affected 425 million patients in 2017. The World Health Organization predicts that diabetes will become the seventh leading cause of death by 2030[32]. The major cause of morbidity and mortality in people with diabetes is CVDs. Adults with diabetes face a 2-4 times higher cardiovascular risk compared to those without diabetes[33]. Type 1 DM, characterized by beta cell failure in pancreatic islets and decreased insulin release, is prevalent among teenagers and children[34]. On the other hand, type 2 DM (T2DM), defined by insulin resistance and hyperglycemia, is non-insulin dependent[35]. While T2DM is predominantly observed in adults, there is an increasing incidence among children due to the rising prevalence of obesity[36].

Throughout history, numerous drugs have been derived from the use of medicinal plants. Plants exhibiting effective pharmacological effects with minimal side reactions are preferred for various diseases due to advantages such as economic feasibility and accessibility[37]. This review article highlights medicinal plants' effectiveness on vasorelaxation

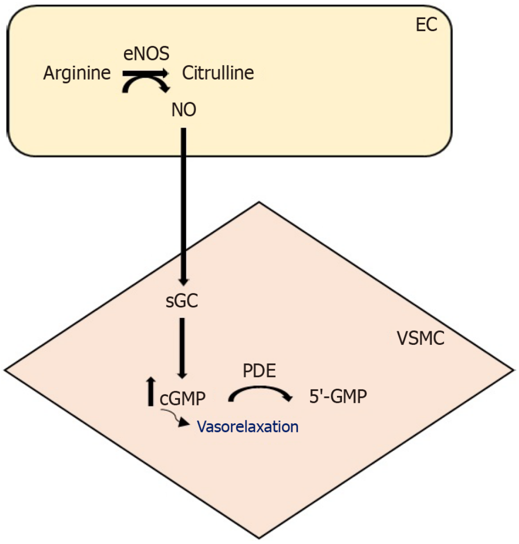

Figure 3 Vasorelaxation effect of phosphodiesterases inhibition. cGMP: Cyclic guanosine monophosphate; EC: Endothelial cell; eNOS: Endothelial nitric oxide synthase; 5'-GMP: 5'-Guanylic acid; NO: Nitric oxide; PDE: Phosphodiesterase; sGC: Soluble guanylate cyclase; VSMC: Vascular smooth muscle cell.

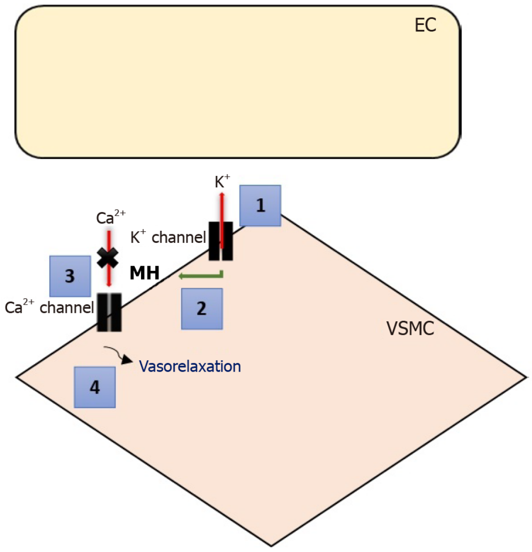

Figure 4 Vasorelaxation effect of opening K^+ ion channels/reduction of Ca^{2+} levels in the cell. EC: Endothelial cell; MH: Membrane hyperpolarization; VSMC: Vascular smooth muscle cell.

and diabetes, emphasizing their potential benefits for CVDs. Given the lack of existing literature on medicinal plants' impact on vasorelaxation and diabetes, this review aims to address this knowledge gap[38] (Figure 4).

MEDICINAL PLANTS AND THEIR FORMATIONS WITH BOTH VASORELAXANT ACTIONS AND AFFIRMATIVE EFFECTS ON DIABETES

This section focuses on medicinal plants related to vasorelaxation and diabetes, as presented in Table 1. Each herb, identified by its binomial name, categorizes its effects concerning vasorelaxation and diabetes. Formations such as extracts, fractions, compounds, flavonoids, oils, formulations, and polysaccharides obtained from each medicinal plant are detailed in the table. Examples include the methanolic extract from *Bauhinia forficata* Link[39], n-butanol fraction from *Mentha longifolia*[40], compounds 1-4, 7, 8, and 16 from *Plumeria rubra*[41], total flavonoids from *Euphorbia humifusa* Willd [42], essential oil from *Alpinia zerumbet*[43], formulation from *Bidens Pilosa*[44], and polysaccharide from *Coptis chinensis* [38].

The table indicates whether vasorelaxation is linked to the endothelium or not, and pathways and channels are also highlighted, such as *Gynura procumbens*[45], *Morus alba*[46], *Prunus mume* Sieb. et Zucc[47], *Swietenia macrophylla* King[48].

Moreover, medicinal plants exhibit diverse specialties in diabetes (Table 1). Examples include anti-diabetic effects with *Terminalia superba*[49], anti-hyperglycemic effects with *Gmelina arborea*[50], hypoglycemic effects with *Vitex agnus-castus* [51], anti-glycation effects with *Echinodorus grandifloras*[52], α-glucosidase inhibitor activity with *Coriandrum sativum*[53], α -amylase inhibitor activity with *Vernonia amygdalina*[54], protein tyrosine phosphatase 1B (PTP1B) inhibition with *Rubus chingii*[55], ß-galactosidase inhibition with *Haloxylon scoparium*[56], and diacylglycerol acyltransferase-1 (DGAT1) inhibitory effects with *Psoralea corylifolia* L[57].

In addition, Table 1 demonstrates that medicinal herbs possess desirable efficacies on diabetic nephropathy, diabetic cardiomyopathy, and prediabetes, exemplified by *Ligusticum chuanxiong* Hort[58], *Jasminum sambac*[59], and *Apium graveolens* L[60], respectively (Table 1[61-204]).

CONCLUSION

This review article delves into the intersection of vasorelaxation and diabetes within the realm of medicinal plants. Each medicinal herb examined here is intricately connected with both topics, with the overarching aim of providing a promising perspective on cardiovascular disorders. The study reports on various vasorelaxant action mechanisms, encompassing endothelium-dependent and -independent vasorelaxation, observed in various experimental studies in conjunction with medicinal plants.

The review highlights that several medicinal herbs can mitigate the undesirable effects of diabetes, drawing upon extensive literature scans. These herbs exhibit a spectrum of properties, including being anti-diabetic, anti-hyperglycemic, hypoglycemic, promoting insulin expression, anti-glycation, alpha-glucosidase inhibition, α-amylase inhibition, PTP1B inhibition, ß-galactosidase inhibition, and DGAT1 inhibition. Furthermore, the study underscores the influence of medicinal plants on affirmative outcomes in diabetic nephropathy, diabetic cardiomyopathy, and pre-diabetic conditions. In studies focusing on the anti-diabetic activity of medicinal plants, an effectiveness rate of 81% is observed when plant selection is based on ethnobotanical records and traditional folk use. However, this rate decreases to 47% in the case of random plant selection[205]. Most studies investigating the efficacy of medicinal plants on diabetes reveal that total plant extract is more effective than pure secondary metabolites in the extract composition[206].

The reported effects on vasorelaxation and diabetes encompass a wide array of plant components, such as extracts, compounds, fractions, oils, formulations, flavonoids, and polysaccharides, derived from various parts of these plants. To the best of our knowledge, this study is pioneering, offering a unique perspective that addresses both vasorelaxation and diabetes concerning medicinal plants. The comprehensive collection of medicinal plant references presented in this study is anticipated to serve as a valuable resource, inspiring and guiding future investigations into CVDs and diabetes.

In this study, 85 species from 79 genera across 41 plant families were investigated. The majority of the medicinal plants examined belong to families such as Lamiaceae, Fabaceae, Rosaceae, Apiaceae, and Asteraceae, implying a potentially higher therapeutic efficacy in treating and preventing cardiovascular diseases compared to other families. Moreover, employing species from these families in cardiovascular disease studies could result in cost and time savings. The plant species and their respective families are presented in Table 2 for reference.

Table 2 Familial classification of various medicinal plants with vasorelaxant activities and beneficial effects on diabetes

Fabaceae	Lamiaceae	Rosaceae	Brassicaceae	Myrtaceae
Securigera securidaca L.; *Parkia biglobosa*; *Bauhinia forficata* Link; *Dalbergia odorifera* T. Chen; *Glycyrrhiza uralensis*; *Sophora alopecuroides*; *Sophora flavescensi*; *Psoralea corylifolia* L.	*Orthosiphon stamineus*; *Thymus linearis* Benth; *Gmelina arborea*; *Vitex agnus-castus*; *Ocimum gratissimum*; *Marrubium vulgare*; *Salvia miltiorrhiza*; *Mentha longifolia*; *Scutellaria baicalensis* Georgi; *Ajuga iva* (L.) Schreber	*Rosa damascena* Mill.; *Sorbus commixta* Hedl.; *Aronia melanocarpa*; *P. mume* Sieb. et Zucc.; *Prunus persica*; *P. yedoensis* Matsum.; *Rubus chingii*	*Eruca sativa* Mill.	*Eucalyptus globulus*; *Myrciaria cauliflora* Berg; *Myrtus communis* L.
Alismataceae	Asteraceae	Nelumbonaceae	Clusiaceae	Apocynaceae
Echinodorus grandiflorus	*Gynura procumbens*; *E. breviscapus* Hand Mazz.; *Vernonia amygdalina*; *Artemisia herba alba*; *Bidens pilosa*	*Nelumbo nucifera*	*Garcinia cowa*	*Plumeria rubra*; *Hancornia speciosa* Gomes
Iridaceae	Moraceae	Apiaceae	Annonaceae	Sapindaceae
Crocus sativus L.	*Morus alba*; *Morus bombycis* Koidzumi	*Coriandrum sativum*; *Angelica decursiva*; *Apium graveolens* L.; *Petroselinum crispum*; *L. chuanxiong* Hort.; *Angelica keiskei*	*Annona squamosal*	*Xanthoceras sorbifolia* Bunge
Poaceae	Bignoniaceae	Euphorbiaceae	Zingiberaceae	Passifloraceae
Cymbopogon martinii	*Mansoa hirsuta* D.C.	*E. humifusa* Willd.	*Kaempferia parviflora*; *Kaempferia galanga* L.; *Curcuma longa*; *Alpinia zerumbet*	*Passiflora edulis*

Rubiaceae	Plantaginaceae	Amaranthaceae	Meliaceae	Phyllanthaceae
Hintonia latiflora	*Bacopa monnieri; Globularia alypum*	*Haloxylon scoparium*	*S. macrophylla* King	*Phyllanthus niruri* L.
Moringaceae	Ginkgoaceae	Amaryllidaceae	Paeoniaceae	Ranunculaceae
Moringa oleifera	*Ginkgo biloba*	*Allium sativum; Allium cepa*	*P. suffruticosa* Andr.	*Nigella sativa; Coptis chinensis; Cimicifuga racemosa*
Cannabaceae	Pedaliaceae	Malvaceae	Oleaceae	Acanthaceae
Humulus lupulus L.	*Sesamum indicum* L.	*Hibiscus sabdariffa; Guazuma ulmifolia*	*Jasminum sambac*	*P. palatiferum*
Combretaceae	Lauraceae	Capparaceae	Polygonaceae	Menispermaceae
Terminalia superba; Anogeissus leiocarpus	*Persea americana* Mill.	*Capparis aphylla*	*Rheum undulatum*	*Coscinium fenestratum*
Rutaceae				
Z. armatum DC				

FOOTNOTES

Author contributions: Demirel S designed the project and wrote the manuscript.

Conflict-of-interest statement: The authors declare that they have no conflict of interest to disclose.

Country/Territory of origin: Türkiye

ORCID number: Sadettin Demirel 0000-0002-3629-5344.

S-Editor: Chen YL
L-Editor: A
P-Editor: Zheng XM

REFERENCES

1 **Balakumar P**, Maung-U K, Jagadeesh G. Prevalence and prevention of cardiovascular disease and diabetes mellitus. *Pharmacol Res* 2016; **113**: 600-609 [PMID: 27697647 DOI: 10.1016/j.phrs.2016.09.040]

2 **Marziano C**, Genet G, Hirschi KK. Vascular endothelial cell specification in health and disease. *Angiogenesis* 2021; **24**: 213-236 [PMID: 33844116 DOI: 10.1007/s10456-021-09785-7]

3 **Gao Y**. Architecture of the Blood Vessels. In: Gao Y, editor. Biology of Vascular Smooth Muscle: Vasoconstriction and Dilatation. Singapore: Springer Nature Singapore, 2022: 3-17 [DOI: 10.1007/978-981-19-7122-8_1]

4 **Krüger-Genge A**, Blocki A, Franke RP, Jung F. Vascular Endothelial Cell Biology: An Update. *Int J Mol Sci* 2019; **20** [PMID: 31500313 DOI: 10.3390/ijms20184411]

5 **Petrie JR**, Guzik TJ, Touyz RM. Diabetes, Hypertension, and Cardiovascular Disease: Clinical Insights and Vascular Mechanisms. *Can J Cardiol* 2018; **34**: 575-584 [PMID: 29459239 DOI: 10.1016/j.cjca.2017.12.005]

6 **Li Y**, Liu Y, Liu S, Gao M, Wang W, Chen K, Huang L. Diabetic vascular diseases: molecular mechanisms and therapeutic strategies. *Signal Transduct Target Ther* 2023; **8**: 152 [PMID: 37037849 DOI: 10.1038/s41392-023-01400-z]

7 **Peng Z**, Shu B, Zhang Y, Wang M. Endothelial Response to Pathophysiological Stress. *Arterioscler Thromb Vasc Biol* 2019; **39**: e233-e243 [PMID: 31644356 DOI: 10.1161/ATVBAHA.119.312580]

8 **Theofilis P**, Sagris M, Oikonomou E, Antonopoulos AS, Siasos G, Tsioufis C, Tousoulis D. Inflammatory Mechanisms Contributing to Endothelial Dysfunction. *Biomedicines* 2021; **9** [PMID: 34356845 DOI: 10.3390/biomedicines9070781]

9 **Gao Y**. Endothelium-Derived Factors. In: Gao Y, editor. Biology of Vascular Smooth Muscle: Vasoconstriction and Dilatation. Singapore: Springer Nature Singapore, 2022: 131-152 [DOI: 10.1007/978-981-19-7122-8_8]

10 **Bartáková A**, Nováková M. Secondary Metabolites of Plants as Modulators of Endothelium Functions. *Int J Mol Sci* 2021; **22** [PMID: 33802468 DOI: 10.3390/ijms22052533]

11 **Rajendran P**, Rengarajan T, Thangavel J, Nishigaki Y, Sakthisekaran D, Sethi G, Nishigaki I. The vascular endothelium and human diseases. *Int J Biol Sci* 2013; **9**: 1057-1069 [PMID: 24250251 DOI: 10.7150/ijbs.7502]

12 **Luna-Vázquez FJ**, Ibarra-Alvarado C, Camacho-Corona MDR, Rojas-Molina A, Rojas-Molina JI, García A, Bah M. Vasodilator Activity of Compounds Isolated from Plants Used in Mexican Traditional Medicine. *Molecules* 2018; **23** [PMID: 29912156 DOI:

10.3390/molecules23061474]
13 **Guerrero EI**, Morán-Pinzón JA, Ortíz LG, Olmedo D, del Olmo E, López-Pérez JL, San Feliciano A, Gupta MP. Vasoactive effects of different fractions from two Panamanians plants used in Amerindian traditional medicine. *J Ethnopharmacol* 2010; **131**: 497-501 [PMID: 20600752 DOI: 10.1016/j.jep.2010.06.036]
14 **Luna-Vázquez FJ**, Ibarra-Alvarado C, Rojas-Molina A, Rojas-Molina I, Zavala-Sánchez MA. Vasodilator compounds derived from plants and their mechanisms of action. *Molecules* 2013; **18**: 5814-5857 [PMID: 23685938 DOI: 10.3390/molecules18055814]
15 **Capettini LS**, Campos LV, Dos Santos MH, Nagem TJ, Lemos VS, Cortes SF. Vasodilator and antioxidant effect of xanthones isolated from Brazilian medicinal plants. *Planta Med* 2009; **75**: 145-148 [PMID: 19090455 DOI: 10.1055/s-0028-1088388]
16 **Tang F**, Yan HL, Wang LX, Xu JF, Peng C, Ao H, Tan YZ. Review of Natural Resources With Vasodilation: Traditional Medicinal Plants, Natural Products, and Their Mechanism and Clinical Efficacy. *Front Pharmacol* 2021; **12**: 627458 [PMID: 33867985 DOI: 10.3389/fphar.2021.627458]
17 **Malekmohammad K**, Sewell RDE, Rafieian-Kopaei M. Mechanisms of Medicinal Plant Activity on Nitric Oxide (NO) Bioavailability as Prospective Treatments for Atherosclerosis. *Curr Pharm Des* 2020; **26**: 2591-2601 [PMID: 32188375 DOI: 10.2174/1381612826666200318152049]
18 **Kadir MF**, Bin Sayeed MS, Shams T, Mia MM. Ethnobotanical survey of medicinal plants used by Bangladeshi traditional health practitioners in the management of diabetes mellitus. *J Ethnopharmacol* 2012; **144**: 605-611 [PMID: 23063956 DOI: 10.1016/j.jep.2012.09.050]
19 **Salehi B**, Ata A, V Anil Kumar N, Sharopov F, Ramírez-Alarcón K, Ruiz-Ortega A, Abdulmajid Ayatollahi S, Tsouh Fokou PV, Kobarfard F, Amiruddin Zakaria Z, Iriti M, Taheri Y, Martorell M, Sureda A, Setzer WN, Durazzo A, Lucarini M, Santini A, Capasso R, Ostrander EA; Atta-ur-Rahman, Choudhary MI, Cho WC, Sharifi-Rad J. Antidiabetic Potential of Medicinal Plants and Their Active Components. *Biomolecules* 2019; **9** [PMID: 31575072 DOI: 10.3390/biom9100551]
20 **Trojan-Rodrigues M**, Alves TL, Soares GL, Ritter MR. Plants used as antidiabetics in popular medicine in Rio Grande do Sul, southern Brazil. *J Ethnopharmacol* 2012; **139**: 155-163 [PMID: 22079795 DOI: 10.1016/j.jep.2011.10.034]
21 **Garima S**, Ajit Kumar P, Marcy DM, Sakthivel R, Bhim Pratap S, Nachimuthu Senthil K. Ethnobotanical survey of medicinal plants used in the management of cancer and diabetes. *J Tradit Chin Med* 2020; **40**: 1007-1017 [PMID: 33258353 DOI: 10.19852/j.cnki.jtcm.2020.06.012]
22 **Zhao Y**, Vanhoutte PM, Leung SW. Vascular nitric oxide: Beyond eNOS. *J Pharmacol Sci* 2015; **129**: 83-94 [PMID: 26499181 DOI: 10.1016/j.jphs.2015.09.002]
23 **Montfort WR**, Wales JA, Weichsel A. Structure and Activation of Soluble Guanylyl Cyclase, the Nitric Oxide Sensor. *Antioxid Redox Signal* 2017; **26**: 107-121 [PMID: 26979942 DOI: 10.1089/ars.2016.6693]
24 **Zeng C**, Liu J, Zheng X, Hu X, He Y. Prostaglandin and prostaglandin receptors: present and future promising therapeutic targets for pulmonary arterial hypertension. *Respir Res* 2023; **24**: 263 [PMID: 37915044 DOI: 10.1186/s12931-023-02559-3]
25 **Korbecki J**, Rębacz-Maron E, Kupnicka P, Chlubek D, Baranowska-Bosiacka I. Synthesis and Significance of Arachidonic Acid, a Substrate for Cyclooxygenases, Lipoxygenases, and Cytochrome P450 Pathways in the Tumorigenesis of Glioblastoma Multiforme, Including a Pan-Cancer Comparative Analysis. *Cancers (Basel)* 2023; **15** [PMID: 36765904 DOI: 10.3390/cancers15030946]
26 **Touyz RM**, Alves-Lopes R, Rios FJ, Camargo LL, Anagnostopoulou A, Arner A, Montezano AC. Vascular smooth muscle contraction in hypertension. *Cardiovasc Res* 2018; **114**: 529-539 [PMID: 29394331 DOI: 10.1093/cvr/cvy023]
27 **Muthal AP**, Kulkarni R, Dileep K, Mukherjee-Kandhare CB, Kandhare AD, Ambavade SD, Wagh V, Bodhankar SL. Cyclic adenosine monophosphate: Recent and future perspectives on various diseases. *JAPS* 2022; **12**: 1-15 [DOI: 10.7324/JAPS.2022.120301]
28 **Calamera G**, Moltzau LR, Levy FO, Andressen KW. Phosphodiesterases and Compartmentation of cAMP and cGMP Signaling in Regulation of Cardiac Contractility in Normal and Failing Hearts. *Int J Mol Sci* 2022; **23** [PMID: 35216259 DOI: 10.3390/ijms23042145]
29 **Checchetto V**, Leanza L, De Stefani D, Rizzuto R, Gulbins E, Szabo I. Mitochondrial K(+) channels and their implications for disease mechanisms. *Pharmacol Ther* 2021; **227**: 107874 [PMID: 33930454 DOI: 10.1016/j.pharmthera.2021.107874]
30 **Gao Y**. Intracellular Ca2+ Regulation. In: Gao Y, editor. Biology of Vascular Smooth Muscle: Vasoconstriction and Dilatation. Singapore: Springer Nature Singapore, 2022: 191-211 [DOI: 10.1007/978-981-19-7122-8_11]
31 **Dhoble S**, Patravale V, Weaver E, Lamprou DA, Patravale T. Comprehensive review on novel targets and emerging therapeutic modalities for pulmonary arterial Hypertension. *Int J Pharm* 2022; **621**: 121792 [PMID: 35513217 DOI: 10.1016/j.ijpharm.2022.121792]
32 **Fan W**. Epidemiology in diabetes mellitus and cardiovascular disease. *Cardiovasc Endocrinol* 2017; **6**: 8-16 [PMID: 31646113 DOI: 10.1097/XCE.0000000000000116]
33 **Dal Canto E**, Ceriello A, Rydén L, Ferrini M, Hansen TB, Schnell O, Standl E, Beulens JW. Diabetes as a cardiovascular risk factor: An overview of global trends of macro and micro vascular complications. *Eur J Prev Cardiol* 2019; **26**: 25-32 [PMID: 31722562 DOI: 10.1177/2047487319878371]
34 **Chetan MR**, Thrower SL, Narendran P. What is type 1 diabetes? *Medicine* 2019; **47**: 5-9 [DOI: 10.1383/medc.30.1.1.28264]
35 **Rachdaoui N**. Insulin: The Friend and the Foe in the Development of Type 2 Diabetes Mellitus. *Int J Mol Sci* 2020; **21** [PMID: 32150819 DOI: 10.3390/ijms21051770]
36 **Serbis A**, Giapros V, Kotanidou EP, Galli-Tsinopoulou A, Siomou E. Diagnosis, treatment and prevention of type 2 diabetes mellitus in children and adolescents. *World J Diabetes* 2021; **12**: 344-365 [PMID: 33889284 DOI: 10.4239/wjd.v12.i4.344]
37 **Aware CB**, Patil DN, Suryawanshi SS, Mali PR, Rane MR, Gurav RG, Jadhav JP. Natural bioactive products as promising therapeutics: A review of natural product-based drug development. *S Afr J Bot* 2022; **151**: 512-28 [DOI: 10.1016/j.sajb.2022.05.028]
38 **Cui L**, Liu M, Chang X, Sun K. The inhibiting effect of the Coptis chinensis polysaccharide on the type II diabetic mice. *Biomed Pharmacother* 2016; **81**: 111-119 [PMID: 27261584 DOI: 10.1016/j.biopha.2016.03.038]
39 **Chávez-Bustos EA**, Morales-González A, Anguiano-Robledo L, Madrigal-Santillán EO, Valadez-Vega C, Lugo-Magaña O, Mendoza-Pérez JA, Fregoso-Aguilar TA. Bauhinia forficata Link, Antioxidant, Genoprotective, and Hypoglycemic Activity in a Murine Model. *Plants (Basel)* 2022; **11** [PMID: 36432781 DOI: 10.3390/plants11223052]
40 **Alamgeer**, Asif H, Chohan TA, Irfan HM, Asim MH, Bukhari SNA, Younis W, Althobaiti YS, Ullah A, Khan AQ, Hakami AY. Ex vivo, in vitro, and in silico approaches to unveil the mechanisms underlying vasorelaxation effect of Mentha Longifolia (L.) in porcine coronary artery. *Biomed Pharmacother* 2022; **153**: 113298 [PMID: 35759866 DOI: 10.1016/j.biopha.2022.113298]
41 **Zhang SN**, Song HZ, Ma RJ, Liang CQ, Wang HS, Tan QG. Potential anti-diabetic isoprenoids and a long-chain δ-lactone from frangipani (Plumeria rubra). *Fitoterapia* 2020; **146**: 104684 [PMID: 32634455 DOI: 10.1016/j.fitote.2020.104684]
42 **Wang TT**, Zhou ZQ, Wang S, Ji XW, Wu B, Sun LY, Wen JF, Kang DG, Lee HS, Cho KW, Jin SN. Mechanisms of vasorelaxation induced

by total flavonoids of Euphorbia humifusa in rat aorta. *J Physiol Pharmacol* 2017; **68**: 619-628 [PMID: 29151079]

43 **Rocha DG**, Holanda TM, Braz HLB, de Moraes JAS, Marinho AD, Maia PHF, de Moraes MEA, Fechine-Jamacaru FV, de Moraes Filho MO. Vasorelaxant effect of Alpinia zerumbet's essential oil on rat resistance artery involves blocking of calcium mobilization. *Fitoterapia* 2023; **169**: 105623 [PMID: 37500018 DOI: 10.1016/j.fitote.2023.105623]

44 **Lai BY**, Chen TY, Huang SH, Kuo TF, Chang TH, Chiang CK, Yang MT, Chang CL. Bidens pilosa Formulation Improves Blood Homeostasis and β -Cell Function in Men: A Pilot Study. *Evid Based Complement Alternat Med* 2015; **2015**: 832314 [PMID: 25866541 DOI: 10.1155/2015/832314]

45 **Shahlehi S**, Petalcorin MIR. Activation of cholinergic pathway induced vasodilation in rat aorta using aqueous and methanolic leaf extracts of Gynura procumbens. *Biomed Pharmacother* 2021; **143**: 112066 [PMID: 34560550 DOI: 10.1016/j.biopha.2021.112066]

46 **Panth N**, Paudel KR, Gong DS, Oak MH. Vascular Protection by Ethanol Extract of Morus alba Root Bark: Endothelium-Dependent Relaxation of Rat Aorta and Decrease of Smooth Muscle Cell Migration and Proliferation. *Evid Based Complement Alternat Med* 2018; **2018**: 7905763 [PMID: 30515235 DOI: 10.1155/2018/7905763]

47 **Jo C**, Kim B, Lee K, Choi HY. Vascular Relaxation and Blood Pressure Lowering Effects of Prunus mume in Rats. *Bioengineering (Basel)* 2023; **10** [PMID: 36671646 DOI: 10.3390/bioengineering10010074]

48 **Ch'ng YS**, Loh YC, Tan CS, Ahmad M, Asmawi MZ, Wan Omar WM, Yam MF. Vasodilation and Antihypertensive Activities of Swietenia macrophylla (Mahogany) Seed Extract. *J Med Food* 2018; **21**: 289-301 [PMID: 29420109 DOI: 10.1089/jmf.2017.4008]

49 **Kamtchouing P**, Kahpui SM, Dzeufiet PD, Tédong L, Asongalem EA, Dimo T. Anti-diabetic activity of methanol/methylene chloride stem bark extracts of Terminalia superba and Canarium schweinfurthii on streptozotocin-induced diabetic rats. *J Ethnopharmacol* 2006; **104**: 306-309 [PMID: 16271836 DOI: 10.1016/j.jep.2005.08.075]

50 **Kulkarni YA**, Veeranjaneyulu A. Effects of Gmelina arborea extract on experimentally induced diabetes. *Asian Pac J Trop Med* 2013; **6**: 602-608 [PMID: 23790330 DOI: 10.1016/S1995-7645(13)60104-2]

51 **Ahangarpour A**, Oroojan AA, Khorsandi L, Najimi SA. Pancreatic protective and hypoglycemic effects of Vitex agnus-castus L. fruit hydroalcoholic extract in D-galactose-induced aging mouse model. *Res Pharm Sci* 2017; **12**: 137-143 [PMID: 28515766 DOI: 10.4103/1735-5362.202452]

52 **Franco RR**, da Silva Carvalho D, de Moura FBR, Justino AB, Silva HCG, Peixoto LG, Espindola FS. Antioxidant and anti-glycation capacities of some medicinal plants and their potential inhibitory against digestive enzymes related to type 2 diabetes mellitus. *J Ethnopharmacol* 2018; **215**: 140-146 [PMID: 29274842 DOI: 10.1016/j.jep.2017.12.032]

53 **Brindis F**, González-Andrade M, González-Trujano ME, Estrada-Soto S, Villalobos-Molina R. Postprandial glycaemia and inhibition of α-glucosidase activity by aqueous extract from Coriandrum sativum. *Nat Prod Res* 2014; **28**: 2021-2025 [PMID: 24836119 DOI: 10.1080/14786419.2014.917414]

54 **Patathananone S**, Pothiwan M, Uapipatanakul B, Kunu W. Inhibitory Effects of Vernonia amygdalina Leaf Extracts on Free Radical Scavenging, Tyrosinase, and Amylase Activities. *Prev Nutr Food Sci* 2023; **28**: 302-311 [PMID: 37842258 DOI: 10.3746/pnf.2023.28.3.302]

55 **Zhang XY**, Li W, Wang J, Li N, Cheng MS, Koike K. Protein tyrosine phosphatase 1B inhibitory activities of ursane-type triterpenes from Chinese raspberry, fruits of Rubus chingii. *Chin J Nat Med* 2019; **17**: 15-21 [PMID: 30704618 DOI: 10.1016/S1875-5364(19)30004-4]

56 **Lachkar N**, Lamchouri F, Bouabid K, Boulfia M, Senhaji S, Stitou M, Toufik H. Mineral Composition, Phenolic Content, and In Vitro Antidiabetic and Antioxidant Properties of Aqueous and Organic Extracts of Haloxylon scoparium Aerial Parts. *Evid Based Complement Alternat Med* 2021; **2021**: 9011168 [PMID: 34691229 DOI: 10.1155/2021/9011168]

57 **Zhu G**, Luo Y, Xu X, Zhang H, Zhu M. Anti-diabetic compounds from the seeds of Psoralea corylifolia. *Fitoterapia* 2019; **139**: 104373 [PMID: 31629053 DOI: 10.1016/j.fitote.2019.104373]

58 **Yang WJ**, Li YR, Gao H, Wu XY, Wang XL, Wang XN, Xiang L, Ren DM, Lou HX, Shen T. Protective effect of the ethanol extract from Ligusticum chuanxiong rhizome against streptozotocin-induced diabetic nephropathy in mice. *J Ethnopharmacol* 2018; **227**: 166-175 [PMID: 30176347 DOI: 10.1016/j.jep.2018.08.037]

59 **Umar U**, Ahmed S, Iftikhar A, Iftikhar M, Majeed W, Liaqat A, Shahzad S, Abbas M, Mehmood T, Anwar F. Phenolics Extracted from Jasminum sambac Mitigates Diabetic Cardiomyopathy by Modulating Oxidative Stress, Apoptotic Mediators and the Nfr-2/HO-1 Pathway in Alloxan-Induced Diabetic Rats. *Molecules* 2023; **28** [PMID: 37513325 DOI: 10.3390/molecules28145453]

60 **Yusni Y**, Zufry H, Meutia F, Sucipto KW. The effects of celery leaf (apium graveolens L.) treatment on blood glucose and insulin levels in elderly pre-diabetics. *Saudi Med J* 2018; **39**: 154-160 [PMID: 29436564 DOI: 10.15537/smj.2018.2.21238]

61 **Garjani A**, Fathiazad F, Zakheri A, Akbari NA, Azarmie Y, Fakhrjoo A, Andalib S, Maleki-Dizaji N. The effect of total extract of Securigera securidaca L. seeds on serum lipid profiles, antioxidant status, and vascular function in hypercholesterolemic rats. *J Ethnopharmacol* 2009; **126**: 525-532 [PMID: 19751813 DOI: 10.1016/j.jep.2009.09.003]

62 **Alizadeh-Fanalou S**, Babaei M, Hosseini A, Azadi N, Nazarizadeh A, Shojaii A, Borji M, Malekinejad H, Bahreini E. Effects of Securigera Securidaca seed extract in combination with glibenclamide on antioxidant capacity, fibroblast growth factor 21 and insulin resistance in hyperglycemic rats. *J Ethnopharmacol* 2020; **248**: 112331 [PMID: 31655149 DOI: 10.1016/j.jep.2019.112331]

63 **Ouédraogo S**, Somé N, Ouattara S, Kini FB, Traore A, Bucher B, Guissou IP. Acute toxicity and vascular properties of seed of Parkia biglobosa (JACQ) R. Br Gift (Mimosaceae) on rat aorta. *Afr J Tradit Complement Altern Med* 2012; **9**: 260-265 [PMID: 23983344 DOI: 10.4314/ajtcam.v9i2.12]

64 **Oyedemi SO**, Eze K, Aiyegoro OA, Ibeh RC, Ikechukwu GC, Swain SS, Ejiofor E, Oyedemi BO. Computational, chemical profiling and biochemical evaluation of antidiabetic potential of Parkia biglobosa stem bark extract in type 2 model of rats. *J Biomol Struct Dyn* 2022; **40**: 9948-9961 [PMID: 34180357 DOI: 10.1080/07391102.2021.1938228]

65 **Yam MF**, Tan CS, Ahmad M, Shibao R. Mechanism of vasorelaxation induced by eupatorin in the rats aortic ring. *Eur J Pharmacol* 2016; **789**: 27-36 [PMID: 27370961 DOI: 10.1016/j.ejphar.2016.06.047]

66 **Bassalat N**, Kadan S, Melamed S, Yaron T, Tietel Z, Karam D, Kmail A, Masalha M, Zaid H. In Vivo and In Vitro Antidiabetic Efficacy of Aqueous and Methanolic Extracts of Orthosiphon Stamineus Benth. *Pharmaceutics* 2023; **15** [PMID: 36986806 DOI: 10.3390/pharmaceutics15030945]

67 **Singh MK**, Savita K, Singh S, Mishra D, Rani P, Chanda D, Verma RS. Vasorelaxant property of 2-phenyl ethyl alcohol isolated from the spent floral distillate of damask rose (Rosa damascena Mill.) and its possible mechanism. *J Ethnopharmacol* 2023; **313**: 116603 [PMID: 37149069 DOI: 10.1016/j.jep.2023.116603]

68 **Gholamhoseinian A**, Fallah H, Sharifi far F. Inhibitory effect of methanol extract of Rosa damascena Mill. flowers on alpha-glucosidase activity and postprandial hyperglycemia in normal and diabetic rats. *Phytomedicine* 2009; **16**: 935-941 [PMID: 19380218 DOI:

10.1016/j.phymed.2009.02.020]

69 **Salma U**, Khan T, Shah AJ. Antihypertensive effect of the methanolic extract from Eruca sativa Mill., (Brassicaceae) in rats: Muscarinic receptor-linked vasorelaxant and cardiotonic effects. *J Ethnopharmacol* 2018; **224**: 409-420 [PMID: 29913298 DOI: 10.1016/j.jep.2018.06.013]

70 **Hetta MH**, Owis AI, Haddad PS, Eid HM. The fatty acid-rich fraction of Eruca sativa (rocket salad) leaf extract exerts antidiabetic effects in cultured skeletal muscle, adipocytes and liver cells. *Pharm Biol* 2017; **55**: 810-818 [PMID: 28112007 DOI: 10.1080/13880209.2017.1280687]

71 **de Carvalho ES**, Tirloni CAS, Palozi RAC, Schaedler MI, Guarnier LP, Silva AO, Mota JDS, Cardoso CAL, de Barros ME, Gasparotto Junior A. Endothelium-Dependent Effects of Echinodorus grandiflorus (Cham. & Schltdl.) Micheli Mediated by M3-Muscarinic and B2-Bradykininergic Receptors on Peripheral Vascular Resistance and Its Modulatory Effects on K+ Channels in Mesenteric Vascular Beds. *Evid Based Complement Alternat Med* 2019; **2019**: 4109810 [PMID: 30719059 DOI: 10.1155/2019/4109810]

72 **Tahsin MR**, Tithi TI, Mim SR, Haque E, Sultana A, Bahar NB, Ahmed R, Chowdhury JA, Chowdhury AA, Kabir S, Aktar F, Uddin MS, Amran MS. In Vivo and In Silico Assessment of Diabetes Ameliorating Potentiality and Safety Profile of Gynura procumbens Leaves. *Evid Based Complement Alternat Med* 2022; **2022**: 9095504 [PMID: 35096119 DOI: 10.1155/2022/9095504]

73 **Yorsin S**, Sriwiriyajan S, Chongsa W. Vasorelaxing effect of Garcinia cowa leaf extract in rat thoracic aorta and its underlying mechanisms. *J Tradit Complement Med* 2023; **13**: 219-225 [PMID: 37128198 DOI: 10.1016/j.jtcme.2022.12.001]

74 **Raksat A**, Phukhatmuen P, Yang J, Maneerat W, Charoensup R, Andersen RJ, Wang YA, Pyne SG, Laphookhieo S. Phloroglucinol Benzophenones and Xanthones from the Leaves of Garcinia cowa and Their Nitric Oxide Production and α-Glucosidase Inhibitory Activities. *J Nat Prod* 2020; **83**: 164-168 [PMID: 31860303 DOI: 10.1021/acs.jnatprod.9b00849]

75 **Cechinel-Zanchett CC**, da Silva RCMVAF, Tenfen A, Siebert DA, Micke G, Vitali L, Cechinel-Filho V, Faloni de Andrade S, de Souza P. Bauhinia forficata link, a Brazilian medicinal plant traditionally used to treat cardiovascular disorders, exerts endothelium-dependent and independent vasorelaxation in thoracic aorta of normotensive and hypertensive rats. *J Ethnopharmacol* 2019; **243**: 112118 [PMID: 31351191 DOI: 10.1016/j.jep.2019.112118]

76 **Gong DS**, Kang SW, Sharma K, Kim DW, Oak MH. The Vasorelaxatory Effect of Nelumbo nucifera Spornioderm on Porcine Coronary Artery. *J Nanosci Nanotechnol* 2019; **19**: 1176-1179 [PMID: 30360228 DOI: 10.1166/jnn.2019.15904]

77 **Pipil N**, Gupta PP, Soni S, Chopra D, Lhamo Y, Singh N, Shree B. Hypoglycemic Effect of Nelumbo Nucifera Seed Extract on GLUT-4 mRNA and GLUT-4 Protein in Streptozotocin-Induced Diabetic Rats. *J Pharm Bioallied Sci* 2023; **15**: S1059-S1061 [PMID: 37693992 DOI: 10.4103/jpbs.jpbs_226_23]

78 **Kim EY**, Lee YJ, Rhyu MR. Black cohosh (Cimicifuga racemosa) relaxes the isolated rat thoracic aorta through endothelium-dependent and -independent mechanisms. *J Ethnopharmacol* 2011; **138**: 537-542 [PMID: 22001858 DOI: 10.1016/j.jep.2011.09.048]

79 **Moser C**, Vickers SP, Brammer R, Cheetham SC, Drewe J. Antidiabetic effects of the Cimicifuga racemosa extract Ze 450 in vitro and in vivo in ob/ob mice. *Phytomedicine* 2014; **21**: 1382-1389 [PMID: 25022210 DOI: 10.1016/j.phymed.2014.06.002]

80 **Mancini A**, Serrano-Díaz J, Nava E, D'Alessandro AM, Alonso GL, Carmona M, Llorens S. Crocetin, a carotenoid derived from saffron (Crocus sativus L.), improves acetylcholine-induced vascular relaxation in hypertension. *J Vasc Res* 2014; **51**: 393-404 [PMID: 25531977 DOI: 10.1159/000368930]

81 **Kakouri E**, Agalou A, Kanakis C, Beis D, Tarantilis PA. Crocins from Crocus sativus L. in the Management of Hyperglycemia. In Vivo Evidence from Zebrafish. *Molecules* 2020; **25** [PMID: 33182581 DOI: 10.3390/molecules25225223]

82 **Hsu JH**, Yang CS, Chen JJ. Antioxidant, Anti-α-Glucosidase, Antityrosinase, and Anti-Inflammatory Activities of Bioactive Components from Morus alba. *Antioxidants (Basel)* 2022; **11** [PMID: 36421408 DOI: 10.3390/antiox11112222]

83 **Pan Z**, Feng T, Shan L, Cai B, Chu W, Niu H, Lu Y, Yang B. Scutellarin-induced endothelium-independent relaxation in rat aorta. *Phytother Res* 2008; **22**: 1428-1433 [PMID: 18972583 DOI: 10.1002/ptr.2364]

84 **Su Y**, Fan X, Li S, Li Z, Tian M. Scutellarin Improves Type 2 Diabetic Cardiomyopathy by Regulating Cardiomyocyte Autophagy and Apoptosis. *Dis Markers* 2022; **2022**: 3058354 [PMID: 35571612 DOI: 10.1155/2022/3058354]

85 **Ch'ng YS**, Loh YC, Tan CS, Ahmad M, Asmawi MZ, Wan Omar WM, Yam MF. Vasorelaxant properties of Vernonia amygdalina ethanol extract and its possible mechanism. *Pharm Biol* 2017; **55**: 2083-2094 [PMID: 28832263 DOI: 10.1080/13880209.2017.1357735]

86 **Tan CS**, Ch'ng YS, Loh YC, Zaini Asmawi M, Ahmad M, Yam MF. Vasorelaxation effect of Glycyrrhizae uralensis through the endothelium-dependent Pathway. *J Ethnopharmacol* 2017; **199**: 149-160 [PMID: 28161542 DOI: 10.1016/j.jep.2017.02.001]

87 **Gou SH**, Liu J, He M, Qiang Y, Ni JM. Quantification and bio-assay of α-glucosidase inhibitors from the roots of Glycyrrhiza uralensis Fisch. *Nat Prod Res* 2016; **30**: 2130-2134 [PMID: 26653365 DOI: 10.1080/14786419.2015.1114940]

88 **Lei XL**, Chiou GC. Cardiovascular pharmacology of Panax notoginseng (Burk) F.H. Chen and Salvia miltiorrhiza. *Am J Chin Med* 1986; **14**: 145-152 [PMID: 3799531 DOI: 10.1142/S0192415X86000235]

89 **Carai MA**, Colombo G, Loi B, Zaru A, Riva A, Cabri W, Morazzoni P. Hypoglycemic Effects of a Standardized Extract of Salvia miltiorrhiza Roots in Rats. *Pharmacogn Mag* 2015; **11**: S545-S549 [PMID: 27013792 DOI: 10.4103/0973-1296.172959]

90 **Li N**, Chen Y, Pei Y, Han L, Ren J, Zhou W, Zhou R. Vasorelaxation effect of oxysophoridine on isolated thoracicc aorta rings of rats. *Chin J Physiol* 2021; **64**: 274-280 [PMID: 34975120 DOI: 10.4103/cjp.cjp_60_21]

91 **Song G**, Huang Y, Xiong M, Yang Z, Liu Q, Shen J, Zhao P, Yang X. Aloperine Relieves Type 2 Diabetes Mellitus *via* Enhancing GLUT4 Expression and Translocation. *Front Pharmacol* 2020; **11**: 561956 [PMID: 33568989 DOI: 10.3389/fphar.2020.561956]

92 **Jabeen Q**, Bashir S, Lyoussi B, Gilani AH. Coriander fruit exhibits gut modulatory, blood pressure lowering and diuretic activities. *J Ethnopharmacol* 2009; **122**: 123-130 [PMID: 19146935 DOI: 10.1016/j.jep.2008.12.016]

93 **Li CM**, Guo YQ, Dong XL, Li H, Wang B, Wu JH, Wong MS, Chan SW. Ethanolic extract of rhizome of Ligusticum chuanxiong Hort. (chuanxiong) enhances endothelium-dependent vascular reactivity in ovariectomized rats fed with high-fat diet. *Food Funct* 2014; **5**: 2475-2485 [PMID: 25110278 DOI: 10.1039/c4fo00211c]

94 **Kang DG**, Lee JK, Choi DH, Sohn EJ, Moon MK, Lee HS. Vascular relaxation by the methanol extract of Sorbus cortex *via* NO-cGMP pathway. *Biol Pharm Bull* 2005; **28**: 860-864 [PMID: 15863894 DOI: 10.1248/bpb.28.860]

95 **Na M**, Kim BY, Osada H, Ahn JS. Inhibition of protein tyrosine phosphatase 1B by lupeol and lupenone isolated from Sorbus commixta. *J Enzyme Inhib Med Chem* 2009; **24**: 1056-1059 [PMID: 19548777 DOI: 10.1080/14756360802693312]

96 **Kim JH**, Auger C, Kurita I, Anselm E, Rivoarilala LO, Lee HJ, Lee KW, Schini-Kerth VB. Aronia melanocarpa juice, a rich source of polyphenols, induces endothelium-dependent relaxations in porcine coronary arteries *via* the redox-sensitive activation of endothelial nitric oxide synthase. *Nitric Oxide* 2013; **35**: 54-64 [PMID: 23973200 DOI: 10.1016/j.niox.2013.08.002]

97 **Simeonov SB**, Botushanov NP, Karahanian EB, Pavlova MB, Husianitis HK, Troev DM. Effects of Aronia melanocarpa juice as part of the dietary regimen in patients with diabetes mellitus. *Folia Med (Plovdiv)* 2002; **44**: 20-23 [PMID: 12580526]
98 **Di Giulio C**, Gonzalez Guzman JM, Dutra Gomes JV, Choi YH, Magalhães PO, Fonseca-Bazzo YM, Silveira D, Estrada O. A New Lignan from Annona squamosa L. (Annonaceae) Demonstrates Vasorelaxant Effects In Vitro. *Molecules* 2023; **28** [PMID: 37298733 DOI: 10.3390/molecules28114256]
99 **Ranjana**, Tripathi YB. Insulin secreting and alpha-glucosidase inhibitory activity of hexane extract of Annona squamosa Linn. in streptozotocin (STZ) induced diabetic rats. *Indian J Exp Biol* 2014; **52**: 623-629 [PMID: 24956893]
100 **Naoufel Z**, Hebi M, Ajebli M, Michel JB, Eddouks M. In vitro Vasorelaxant Effect of Artemisia herba alba Asso. in Spontaneously Hypertensive Rats. *Cardiovasc Hematol Agents Med Chem* 2017; **14**: 190-196 [PMID: 27993120 DOI: 10.2174/1871525714666161216100044]
101 **al-Khazraji SM**, al-Shamaony LA, Twaij HA. Hypoglycaemic effect of Artemisia herba alba. I. Effect of different parts and influence of the solvent on hypoglycaemic activity. *J Ethnopharmacol* 1993; **40**: 163-166 [PMID: 8145571 DOI: 10.1016/0378-8741(93)90064-c]
102 **El-Hilaly J**, Lyoussi B, Wibo M, Morel N. Vasorelaxant effect of the aqueous extract of Ajuga iva in rat aorta. *J Ethnopharmacol* 2004; **93**: 69-74 [PMID: 15182907 DOI: 10.1016/j.jep.2004.03.020]
103 **El Hilaly J**, Lyoussi B. Hypoglycaemic effect of the lyophilised aqueous extract of Ajuga iva in normal and streptozotocin diabetic rats. *J Ethnopharmacol* 2002; **80**: 109-113 [PMID: 12007699 DOI: 10.1016/s0378-8741(01)00407-x]
104 **Campana PR**, Braga FC, Cortes SF. Endothelium-dependent vasorelaxation in rat thoracic aorta by Mansoa hirsuta D.C. *Phytomedicine* 2009; **16**: 456-461 [PMID: 19019646 DOI: 10.1016/j.phymed.2008.09.007]
105 **Pereira JR**, Queiroz RF, Siqueira EA, Brasileiro-Vidal AC, Sant'ana AEG, Silva DM, Affonso PRAM. Evaluation of cytogenotoxicity, antioxidant and hypoglycemiant activities of isolate compounds from Mansoa hirsuta D.C. (Bignoniaceae). *An Acad Bras Cienc* 2017; **89**: 317-331 [PMID: 28423086 DOI: 10.1590/0001-3765201720160585]
106 **Bai X**, Aimila A, Aidarhan N, Duan X, Maiwulanjiang M. Chemical constituents and biological activities of essential oil from Mentha longifolia: effects of different extraction methods. *Int J Food Prop* 2020; **23**: 1951-1960 [DOI: 10.1080/10942912.2020.1833035]
107 **Rakotondrabe TF**, Fan M, Guo M. Exploring potential antidiabetic and anti-inflammatory flavonoids from Euphorbia humifusa with an integrated strategy. *Front Pharmacol* 2022; **13**: 980945 [PMID: 36105200 DOI: 10.3389/fphar.2022.980945]
108 **Jin SN**, Wen JF, Li X, Kang DG, Lee HS, Cho KW. The mechanism of vasorelaxation induced by ethanol extract of Sophora flavescens in rat aorta. *J Ethnopharmacol* 2011; **137**: 547-552 [PMID: 21704693 DOI: 10.1016/j.jep.2011.06.013]
109 **Kim JH**, Cho CW, Kim HY, Kim KT, Choi GS, Kim HH, Cho IS, Kwon SJ, Choi SK, Yoon JY, Yang SY, Kang JS, Kim YH. α-Glucosidase inhibition by prenylated and lavandulyl compounds from Sophora flavescens roots and in silico analysis. *Int J Biol Macromol* 2017; **102**: 960-969 [PMID: 28455256 DOI: 10.1016/j.ijbiomac.2017.04.092]
110 **Wattanapitayakul SK**, Chularojmontri L, Herunsalee A, Charuchongkolwongse S, Chansuvanich N. Vasorelaxation and antispasmodic effects of Kaempferia parviflora ethanolic extract in isolated rat organ studies. *Fitoterapia* 2008; **79**: 214-216 [PMID: 18178015 DOI: 10.1016/j.fitote.2007.11.017]
111 **Kim B**, Kwon Y, Lee S, Lee K, Ham I, Choi HY. Vasorelaxant effects of Angelica decursiva root on isolated rat aortic rings. *BMC Complement Altern Med* 2017; **17**: 474 [PMID: 28969672 DOI: 10.1186/s12906-017-1965-z]
112 **Ali MY**, Jannat S, Jung HA, Jeong HO, Chung HY, Choi JS. Coumarins from Angelica decursiva inhibit α-glucosidase activity and protein tyrosine phosphatase 1B. *Chem Biol Interact* 2016; **252**: 93-101 [PMID: 27085377 DOI: 10.1016/j.cbi.2016.04.020]
113 **Vierling C**, Baumgartner CM, Bollerhey M, Erhardt WD, Stampfl A, Vierling W. The vasodilating effect of a Hintonia latiflora extract with antidiabetic action. *Phytomedicine* 2014; **21**: 1582-1586 [PMID: 25442266 DOI: 10.1016/j.phymed.2014.07.009]
114 **Korecova M**, Hladikova M. Treatment of mild and moderate type-2 diabetes: open prospective trial with Hintonia latiflora extract. *Eur J Med Res* 2014; **19**: 16 [PMID: 24678614 DOI: 10.1186/2047-783X-19-16]
115 **Srivastava N**, Mishra S, Iqbal H, Chanda D, Shanker K. Standardization of Kaempferia galanga L. rhizome and vasorelaxation effect of its key metabolite ethyl p-methoxycinnamate. *J Ethnopharmacol* 2021; **271**: 113911 [PMID: 33571614 DOI: 10.1016/j.jep.2021.113911]
116 **Begum T**, Gogoi R, Sarma N, Pandey SK, Lal M. Novel ethyl p-methoxy cinnamate rich Kaempferia galanga (L.) essential oil and its pharmacological applications: special emphasis on anticholinesterase, anti-tyrosinase, α-amylase inhibitory, and genotoxic efficiencies. *PeerJ* 2023; **11**: e14606 [PMID: 36643622 DOI: 10.7717/peerj.14606]
117 **Lee MW**, Kwon JE, Lee YJ, Jeong YJ, Kim I, Cho YM, Kim YM, Kang SC. Prunus mume leaf extract lowers blood glucose level in diabetic mice. *Pharm Biol* 2016; **54**: 2135-2140 [PMID: 26911402 DOI: 10.3109/13880209.2016.1147052]
118 **Kamkaew N**, Paracha TU, Ingkaninan K, Waranuch N, Chootip K. Vasodilatory Effects and Mechanisms of Action of Bacopa monnieri Active Compounds on Rat Mesenteric Arteries. *Molecules* 2019; **24** [PMID: 31208086 DOI: 10.3390/molecules24122243]
119 **Ghosh T**, Maity TK, Singh J. Antihyperglycemic activity of bacosine, a triterpene from Bacopa monnieri, in alloxan-induced diabetic rats. *Planta Med* 2011; **77**: 804-808 [PMID: 21154199 DOI: 10.1055/s-0030-1250600]
120 **Amtaghri S**, Eddouks M. Study of the Antihypertensive and Vasorelaxant Activities of Haloxylon scoparium in Rats. *Cardiovasc Hematol Agents Med Chem* 2023; **21**: 139-153 [PMID: 36017835 DOI: 10.2174/1871525720666220823163542]
121 **Duan JY**, Wang YJ, Chen W, Zhao YQ, Bai ZH, He LL, Zhang CP. Limonoids isolated from fruits of Swietenia macrophylla king enhance glucose consumption in insulin-resistant HepG2 cells *via* activating PPARγ. *J Food Biochem* 2021; **45**: e13668 [PMID: 33605461 DOI: 10.1111/jfbc.13668]
122 **Ajebli M**, Eddouks M. Eucalyptus globulus possesses antihypertensive activity in L-NAME-induced hypertensive rats and relaxes isolated rat thoracic aorta through nitric oxide pathway. *Nat Prod Res* 2021; **35**: 819-821 [PMID: 30966776 DOI: 10.1080/14786419.2019.1598992]
123 **Bokaeian M**, Nakhaee A, Moodi B, Ali Khazaei H. Eucalyptus globulus (eucalyptus) treatment of candidiasis in normal and diabetic rats. *Iran Biomed J* 2010; **14**: 121-126 [PMID: 21079663]
124 **Khan IA**, Hussain M, Syed SK, Saadullah M, Alqahtani AM, Alqahtani T, Aldahish AA, Asiri S, Zeng LH. Pharmacological Justification for the Medicinal Use of Plumeria rubra Linn. in Cardiovascular Disorders. *Molecules* 2021; **27** [PMID: 35011482 DOI: 10.3390/molecules27010251]
125 **Kim B**, Kim KW, Lee S, Jo C, Lee K, Ham I, Choi HY. Endothelium-Dependent Vasorelaxant Effect of Prunus Persica Branch on Isolated Rat Thoracic Aorta. *Nutrients* 2019; **11** [PMID: 31390819 DOI: 10.3390/nu11081816]
126 **Lee K**, Ham I, Yang G, Lee M, Bu Y, Kim H, Choi HY. Vasorelaxant effect of Prunus yedoensis bark. *BMC Complement Altern Med* 2013; **13**: 31 [PMID: 23410148 DOI: 10.1186/1472-6882-13-31]

127 **Jo K**, Lee SE, Lee SW, Hwang JK. Prunus yedoensis Matsum. stimulates glucose uptake in L6 rat skeletal muscle cells by activating AMP-activated protein kinase and phosphatidylinositol 3-kinase/Akt pathways. *Nat Prod Res* 2012; **26**: 1610-1615 [PMID: 21809954 DOI: 10.1080/14786419.2011.574133]

128 **Jin SN**, Wen JF, Kim HY, Kang DG, Lee HS, Cho KW. Vascular relaxation by ethanol extract of Xanthoceras sorbifolia *via* Akt- and SOCE-eNOS-cGMP pathways. *J Ethnopharmacol* 2010; **132**: 240-245 [PMID: 20713148 DOI: 10.1016/j.jep.2010.08.007]

129 **Zhang Y**, Ma JN, Ma CL, Qi Z, Ma CM. Simultaneous quantification of ten constituents of Xanthoceras sorbifolia Bunge using UHPLC-MS methods and evaluation of their radical scavenging, DNA scission protective, and α-glucosidase inhibitory activities. *Chin J Nat Med* 2015; **13**: 873-880 [PMID: 26614463 DOI: 10.1016/S1875-5364(15)30092-3]

130 **Cabral B**, Bortolin RH, Gonçalves TAF, Maciel PMP, de Arruda AV, de Carvalho TG, Abboud KY, Alves JSF, Cordeiro LMC, de Medeiros IA, de Rezende AA, Zucolotto SM. Hypoglycemic and Vasorelaxant Effect of Passiflora edulis Fruit Peel By-Product. *Plant Foods Hum Nutr* 2021; **76**: 466-471 [PMID: 34581915 DOI: 10.1007/s11130-021-00921-8]

131 **Sohrabi F**, Niazmand S, Mahmoudabady M, Niazmand MJ. The vasodilatory effect of Apium graveolens L (celery) seed in isolated rat aorta: The roles of endothelium, calcium and potassium channels. *Avicenna J Phytomed* 2021; **11**: 44-53 [PMID: 33628719]

132 **Iizuka T**, Moriyama H, Nagai M. Vasorelaxant effects of methyl brevifolincarboxylate from the leaves of Phyllanthus niruri. *Biol Pharm Bull* 2006; **29**: 177-179 [PMID: 16394535 DOI: 10.1248/bpb.29.177]

133 **Najari Beidokhti M**, Andersen MV, Eid HM, Sanchez Villavicencio ML, Staerk D, Haddad PS, Jäger AK. Investigation of antidiabetic potential of Phyllanthus niruri L. using assays for α-glucosidase, muscle glucose transport, liver glucose production, and adipogenesis. *Biochem Biophys Res Commun* 2017; **493**: 869-874 [PMID: 28928090 DOI: 10.1016/j.bbrc.2017.09.080]

134 **El Bardai S**, Morel N, Wibo M, Fabre N, Llabres G, Lyoussi B, Quetin-Leclercq J. The vasorelaxant activity of marrubenol and marrubiin from Marrubium vulgare. *Planta Med* 2003; **69**: 75-77 [PMID: 12567286 DOI: 10.1055/s-2003-37042]

135 **Boudjelal A**, Henchiri C, Siracusa L, Sari M, Ruberto G. Compositional analysis and in vivo anti-diabetic activity of wild Algerian Marrubium vulgare L. infusion. *Fitoterapia* 2012; **83**: 286-292 [PMID: 22100836 DOI: 10.1016/j.fitote.2011.11.005]

136 **Kassahun Gebremeskel A**, Wijerathne TD, Kim JH, Kim MJ, Seo CS, Shin HK, Lee KP. Psoralea corylifolia extract induces vasodilation in rat arteries through both endothelium-dependent and -independent mechanisms involving inhibition of TRPC3 channel activity and elaboration of prostaglandin. *Pharm Biol* 2017; **55**: 2136-2144 [PMID: 28982307 DOI: 10.1080/13880209.2017.1383484]

137 **Nishida S**, Satoh H. Comparative vasodilating actions among terpenoids and flavonoids contained in Ginkgo biloba extract. *Clin Chim Acta* 2004; **339**: 129-133 [PMID: 14687903 DOI: 10.1016/j.cccn.2003.10.004]

138 **Cheng D**, Liang B, Li Y. Antihyperglycemic effect of Ginkgo biloba extract in streptozotocin-induced diabetes in rats. *Biomed Res Int* 2013; **2013**: 162724 [PMID: 23509685 DOI: 10.1155/2013/162724]

139 **Su XH**, Duan R, Sun YY, Wen JF, Kang DG, Lee HS, Cho KW, Jin SN. Cardiovascular effects of ethanol extract of Rubus chingii Hu (Rosaceae) in rats: an in vivo and in vitro approach. *J Physiol Pharmacol* 2014; **65**: 417-424 [PMID: 24930514]

140 **Nguelefack TB**, Dimo T, Mbuyo EP, Tan PV, Rakotonirina SV, Kamanyi A. Relaxant effects of the neutral extract of the leaves of Bidens pilosa Linn on isolated rat vascular smooth muscle. *Phytother Res* 2005; **19**: 207-210 [PMID: 15934016 DOI: 10.1002/ptr.1646]

141 **Xuan TD**, Khanh TD. Chemistry and pharmacology of Bidens pilosa: an overview. *J Pharm Investig* 2016; **46**: 91-132 [PMID: 32226639 DOI: 10.1007/s40005-016-0231-6]

142 **Takashima M**, Kanamori Y, Kodera Y, Morihara N, Tamura K. Aged garlic extract exerts endothelium-dependent vasorelaxant effect on rat aorta by increasing nitric oxide production. *Phytomedicine* 2017; **24**: 56-61 [PMID: 28160862 DOI: 10.1016/j.phymed.2016.11.016]

143 **Jini D**, Sharmila S, Anitha A, Pandian M, Rajapaksha RMH. In vitro and in silico studies of silver nanoparticles (AgNPs) from Allium sativum against diabetes. *Sci Rep* 2022; **12**: 22109 [PMID: 36543812 DOI: 10.1038/s41598-022-24818-x]

144 **Ajebli M**, Eddouks M. Antihypertensive activity of Petroselinum crispum through inhibition of vascular calcium channels in rats. *J Ethnopharmacol* 2019; **242**: 112039 [PMID: 31252093 DOI: 10.1016/j.jep.2019.112039]

145 **Yanardağ R**, Bolkent S, Tabakoğlu-Oğuz A, Ozsoy-Saçan O. Effects of Petroselinum crispum extract on pancreatic B cells and blood glucose of streptozotocin-induced diabetic rats. *Biol Pharm Bull* 2003; **26**: 1206-1210 [PMID: 12913280 DOI: 10.1248/bpb.26.1206]

146 **Chen JF**, Liu F, Qiao MM, Shu HZ, Li XC, Peng C, Xiong L. Vasorelaxant effect of curcubisabolanin A isolated from Curcuma longa through the PI3K/Akt/eNOS signaling pathway. *J Ethnopharmacol* 2022; **294**: 115332 [PMID: 35525529 DOI: 10.1016/j.jep.2022.115332]

147 **Wickenberg J**, Ingemansson SL, Hlebowicz J. Effects of Curcuma longa (turmeric) on postprandial plasma glucose and insulin in healthy subjects. *Nutr J* 2010; **9**: 43 [PMID: 20937162 DOI: 10.1186/1475-2891-9-43]

148 **Naseri MK**, Arabian M, Badavi M, Ahangarpour A. Vasorelaxant and hypotensive effects of Allium cepa peel hydroalcoholic extract in rat. *Pak J Biol Sci* 2008; **11**: 1569-1575 [PMID: 18819643 DOI: 10.3923/pjbs.2008.1569.1575]

149 **Bang MA**, Kim HA, Cho YJ. Alterations in the blood glucose, serum lipids and renal oxidative stress in diabetic rats by supplementation of onion (Allium cepa. Linn). *Nutr Res Pract* 2009; **3**: 242-246 [PMID: 20090891 DOI: 10.4162/nrp.2009.3.3.242]

150 **Chompoo J**, Upadhyay A, Kishimoto W, Makise T, Tawata S. Advanced glycation end products inhibitors from Alpinia zerumbet rhizomes. *Food Chem* 2011; **129**: 709-715 [PMID: 25212289 DOI: 10.1016/j.foodchem.2011.04.034]

151 **Kang DG**, Moon MK, Choi DH, Lee JK, Kwon TO, Lee HS. Vasodilatory and anti-inflammatory effects of the 1,2,3,4,6-penta-O-galloyl-beta-D-glucose (PGG) *via* a nitric oxide-cGMP pathway. *Eur J Pharmacol* 2005; **524**: 111-119 [PMID: 16253226 DOI: 10.1016/j.ejphar.2005.08.061]

152 **Zhang MH**, Feng L, Zhu MM, Gu JF, Jiang J, Cheng XD, Ding SM, Wu C, Jia XB. The anti-inflammation effect of Moutan Cortex on advanced glycation end products-induced rat mesangial cells dysfunction and High-glucose-fat diet and streptozotocin-induced diabetic nephropathy rats. *J Ethnopharmacol* 2014; **151**: 591-600 [PMID: 24269777 DOI: 10.1016/j.jep.2013.11.015]

153 **Niazmand S**, Fereidouni E, Mahmoudabady M, Mousavi SM. Endothelium-independent vasorelaxant effects of hydroalcoholic extract from Nigella sativa seed in rat aorta: the roles of Ca2+ and K+ channels. *Biomed Res Int* 2014; **2014**: 247054 [PMID: 24900958 DOI: 10.1155/2014/247054]

154 **Meddah B**, Ducroc R, El Abbes Faouzi M, Eto B, Mahraoui L, Benhaddou-Andaloussi A, Martineau LC, Cherrah Y, Haddad PS. Nigella sativa inhibits intestinal glucose absorption and improves glucose tolerance in rats. *J Ethnopharmacol* 2009; **121**: 419-424 [PMID: 19061948 DOI: 10.1016/j.jep.2008.10.040]

155 **Lobo de Andrade DM**, Reis Cde F, Castro PF, Borges LL, Amaral NO, Torres IM, Rezende SG, Gil Ede S, Cardoso da Conceição E, Pedrino GR, Lavorenti Rocha M. Vasorelaxant and Hypotensive Effects of Jaboticaba Fruit (Myrciaria cauliflora) Extract in Rats. *Evid Based Complement Alternat Med* 2015; **2015**: 696135 [PMID: 25960756 DOI: 10.1155/2015/696135]

156 **Hsu JD**, Wu CC, Hung CN, Wang CJ, Huang HP. Myrciaria cauliflora extract improves diabetic nephropathy *via* suppression of oxidative stress and inflammation in streptozotocin-nicotinamide mice. *J Food Drug Anal* 2016; **24**: 730-737 [PMID: 28911610 DOI: 10.1016/j.jfda.2016.03.009]

157 **Oh KS**, Han W, Wang MH, Lee BH. The effects of chronic treatment with Morus bombycis KOIDZUMI in spontaneously hypertensive rats. *Biol Pharm Bull* 2007; **30**: 1278-1283 [PMID: 17603167 DOI: 10.1248/bpb.30.1278]

158 **Heo SI**, Jin YS, Jung MJ, Wang MH. Antidiabetic properties of 2,5-dihydroxy-4,3'-di(beta-D-glucopyranosyloxy)-trans-stilbene from mulberry (Morus bombycis koidzumi) root in streptozotocin-induced diabetic rats. *J Med Food* 2007; **10**: 602-607 [PMID: 18158829 DOI: 10.1089/jmf.2006.0241]

159 **Figard H**, Girard C, Mougin F, Demougeot C, Berthelot A. Effects of aqueous hop (Humulus Lupulus L.) extract on vascular reactivity in rats: mechanisms and influence of gender and hormonal status. *Phytomedicine* 2008; **15**: 185-193 [PMID: 17951040 DOI: 10.1016/j.phymed.2007.09.016]

160 **Liu M**, Yin H, Liu G, Dong J, Qian Z, Miao J. Xanthohumol, a prenylated chalcone from beer hops, acts as an α-glucosidase inhibitor in vitro. *J Agric Food Chem* 2014; **62**: 5548-5554 [PMID: 24897556 DOI: 10.1021/jf500426z]

161 **Suresh Kumar P**, Patel JS, Saraf MN. Mechanism of vasorelaxant activity of a fraction of root extract of Sesamum indicum Linn. *Indian J Exp Biol* 2008; **46**: 457-464 [PMID: 18697605]

162 **Zheoat AM**, Gray AI, Igoli JO, Ferro VA, Drummond RM. Hibiscus acid from Hibiscus sabdariffa (Malvaceae) has a vasorelaxant effect on the rat aorta. *Fitoterapia* 2019; **134**: 5-13 [PMID: 30690125 DOI: 10.1016/j.fitote.2019.01.012]

163 **Mohamed AI**, Salau VF, Erukainure OL, Islam MS. Hibiscus sabdariffa L. polyphenolic-rich extract promotes muscle glucose uptake and inhibits intestinal glucose absorption with concomitant amelioration of Fe(2+) -induced hepatic oxidative injury. *J Food Biochem* 2022; **46**: e14399 [PMID: 36259155 DOI: 10.1111/jfbc.14399]

164 **Khan IA**, Hussain M, Munawar SH, Iqbal MO, Arshad S, Manzoor A, Shah MA, Abbas K, Shakeel W, Syed SK. Jasminum sambac: A Potential Candidate for Drug Development to Cure Cardiovascular Ailments. *Molecules* 2021; **26** [PMID: 34577135 DOI: 10.3390/molecules26185664]

165 **Ferreira HC**, Serra CP, Lemos VS, Braga FC, Cortes SF. Nitric oxide-dependent vasodilatation by ethanolic extract of Hancornia speciosa *via* phosphatidyl-inositol 3-kinase. *J Ethnopharmacol* 2007; **109**: 161-164 [PMID: 16890389 DOI: 10.1016/j.jep.2006.06.009]

166 **Tomazi R**, Figueira ÂC, Ferreira AM, Ferreira DQ, de Souza GC, de Souza Pinheiro WB, Pinheiro Neto JR, da Silva GA, de Lima HB, da Silva Hage-Melim LI, Pereira ACM, Carvalho JCT, da Silva de Almeida SSM. Hypoglycemic Activity of Aqueous Extract of Latex from Hancornia speciosa Gomes: A Study in Zebrafish and In Silico. *Pharmaceuticals (Basel)* 2021; **14** [PMID: 34577555 DOI: 10.3390/ph14090856]

167 **Khonsung P**, Panthong A, Chiranthanut N, Intahphuak S. Hypotensive effect of the water extract of the leaves of Pseuderanthemum palatiferum. *J Nat Med* 2011; **65**: 551-558 [PMID: 21556972 DOI: 10.1007/s11418-011-0540-z]

168 **Padee P**, Nualkaew S, Talubmook C, Sakuljaitrong S. Hypoglycemic effect of a leaf extract of Pseuderanthemum palatiferum (Nees) Radlk. in normal and streptozotocin-induced diabetic rats. *J Ethnopharmacol* 2010; **132**: 491-496 [PMID: 20813181 DOI: 10.1016/j.jep.2010.07.056]

169 **Tom EN**, Girard C, Dimo T, Mbafor JT, Berthelot A, Demougeot C. Vasorelaxant effects of extracts of the stem bark of Terminalia superba Engler & Diels (Combretaceae). *J Ethnopharmacol* 2010; **127**: 335-340 [PMID: 19897023 DOI: 10.1016/j.jep.2009.10.036]

170 **Magos GA**, Mateos JC, Páez E, Fernández G, Lobato C, Márquez C, Enríquez RG. Hypotensive and vasorelaxant effects of the procyanidin fraction from Guazuma ulmifolia bark in normotensive and hypertensive rats. *J Ethnopharmacol* 2008; **117**: 58-68 [PMID: 18314282 DOI: 10.1016/j.jep.2008.01.015]

171 **Alonso-Castro AJ**, Salazar-Olivo LA. The anti-diabetic properties of Guazuma ulmifolia Lam are mediated by the stimulation of glucose uptake in normal and diabetic adipocytes without inducing adipogenesis. *J Ethnopharmacol* 2008; **118**: 252-256 [PMID: 18487028 DOI: 10.1016/j.jep.2008.04.007]

172 **Ojewole JA**, Kamadyaapa DR, Gondwe MM, Moodley K, Musabayane CT. Cardiovascular effects of Persea americana Mill (Lauraceae) (avocado) aqueous leaf extract in experimental animals. *Cardiovasc J Afr* 2007; **18**: 69-76 [PMID: 17497042]

173 **Lima CR**, Vasconcelos CF, Costa-Silva JH, Maranhão CA, Costa J, Batista TM, Carneiro EM, Soares LA, Ferreira F, Wanderley AG. Anti-diabetic activity of extract from Persea americana Mill. leaf *via* the activation of protein kinase B (PKB/Akt) in streptozotocin-induced diabetic rats. *J Ethnopharmacol* 2012; **141**: 517-525 [PMID: 22472105 DOI: 10.1016/j.jep.2012.03.026]

174 **Shah AJ**, Gilani AH. Blood pressure lowering effect of the extract of aerial parts of Capparis aphylla is mediated through endothelium-dependent and independent mechanisms. *Clin Exp Hypertens* 2011; **33**: 470-477 [PMID: 21978026 DOI: 10.3109/10641963.2010.549273]

175 **Dangi KS**, Mishra SN. Antihyperglycemic, antioxidant and hypolipidemic effect of Capparis aphylla stem extract in streptozotocin induced diabetic rats. *Biology and Medicine* 2010; **2**: 35-44

176 **Yoo MY**, Oh KS, Lee JW, Seo HW, Yon GH, Kwon DY, Kim YS, Ryu SY, Lee BH. Vasorelaxant effect of stilbenes from rhizome extract of rhubarb (Rheum undulatum) on the contractility of rat aorta. *Phytother Res* 2007; **21**: 186-189 [PMID: 17128434 DOI: 10.1002/ptr.2042]

177 **Ha MT**, Park DH, Shrestha S, Kim M, Kim JA, Woo MH, Choi JS, Min BS. PTP1B inhibitory activity and molecular docking analysis of stilbene derivatives from the rhizomes of Rheum undulatum L. *Fitoterapia* 2018; **131**: 119-126 [PMID: 30352293 DOI: 10.1016/j.fitote.2018.10.020]

178 **Chokri A**, El Abida K, Zegzouti YF, Ben Cheikh R. Endothelium-dependent vascular relaxation induced by Globularia alypum extract is mediated by EDHF in perfused rat mesenteric arterial bed. *Can J Physiol Pharmacol* 2012; **90**: 607-616 [PMID: 22530963 DOI: 10.1139/y2012-035]

179 **Tiss M**, Hamden K. Globularia alypum Extracts Attenuate Hyperglycemia and Protect against Various Organ Toxicities in Alloxan-Induced Experimental Diabetic Rats. *Evid Based Complement Alternat Med* 2022; **2022**: 6816942 [PMID: 36082185 DOI: 10.1155/2022/6816942]

180 **Wansi SL**, Nyadjeu P, Nguelefack TB, Fodouop SF, Donatien AA, Kamanyi A. In vivo antioxidant and vasodilating activities of Gmelina arborea (Verberaceae) leaves hexane extract. *J Complement Integr Med* 2012; **9** [PMID: 23045387 DOI: 10.1515/1553-3840.1623]

181 **Wongcome T**, Panthong A, Jesadanont S, Kanjanapothi D, Taesotikul T, Lertprasertsuke N. Hypotensive effect and toxicology of the extract from Coscinium fenestratum (Gaertn.) Colebr. *J Ethnopharmacol* 2007; **111**: 468-475 [PMID: 17229538 DOI: 10.1016/j.jep.2006.12.019]

182 **Punitha IS**, Rajendran K, Shirwaikar A. Alcoholic stem extract of Coscinium fenestratum regulates carbohydrate metabolism and improves antioxidant status in streptozotocin-nicotinamide induced diabetic rats. *Evid Based Complement Alternat Med* 2005; **2**: 375-381 [PMID: 16136216 DOI: 10.1093/ecam/neh099]

183 **Janbaz KH**, Nisa M, Saqib F, Imran I, Zia-Ul-Haq M, De Feo V. Bronchodilator, vasodilator and spasmolytic activities of methanolic extract of Myrtus communis L. *J Physiol Pharmacol* 2013; **64**: 479-484 [PMID: 24101394]

184 **Sepici A**, Gürbüz I, Cevik C, Yesilada E. Hypoglycaemic effects of myrtle oil in normal and alloxan-diabetic rabbits. *J Ethnopharmacol* 2004; **93**: 311-318 [PMID: 15234770 DOI: 10.1016/j.jep.2004.03.049]

185 **Alamgeer**, Auger C, Chabert P, Lugnier C, Mushtaq MN, Schini-Kerth VB. Mechanisms underlying vasorelaxation induced in the porcine coronary arteries by Thymus linearis, Benth. *J Ethnopharmacol* 2018; **225**: 211-219 [PMID: 30009977 DOI: 10.1016/j.jep.2018.07.010]

186 **Younatan Y**, Majid M, Phull AR, Baig MW, Irshad N, Fatima H, Nasir B, Zafar A, Majid A, Parveen A, Haq IU. Thymus linearis Extracts Ameliorate Indices of Metabolic Syndrome in Sprague Dawley Rats. *Oxid Med Cell Longev* 2023; **2023**: 5648837 [PMID: 37151604 DOI: 10.1155/2023/5648837]

187 **Thaçi S**, Krasniqi B, Dërmaku-Sopjani M, Rifati-Nixha A, Abazi S, Sopjani M. Vasorelaxant Effects of the Vitex Agnus-Castus Extract. *Evid Based Complement Alternat Med* 2022; **2022**: 7708781 [PMID: 35360656 DOI: 10.1155/2022/7708781]

188 **Belemnaba L**, Ouédraogo S, Nitiéma M, Chataigneau T, Guissou IP, Schini-Kerth VB, Bucher B, Auger C. An aqueous extract of the Anogeissus leiocarpus bark (AEAL) induces the endothelium-dependent relaxation of porcine coronary artery rings involving predominantly nitric oxide. *J Basic Clin Physiol Pharmacol* 2018; **29**: 599-608 [PMID: 29723154 DOI: 10.1515/jbcpp-2017-0084]

189 **Motto AE**, Lawson-Evi P, Eklu-Gadegbeku K. Antidiabetic and antioxidant potential of total extract and supernatant fraction of the roots of Anogeissus leiocarpus in HFD-fed and Streptozocin -induced diabetic rats. *Biomed Pharmacother* 2022; **154**: 113578 [PMID: 36027612 DOI: 10.1016/j.biopha.2022.113578]

190 **Mushtaq MN**, Ghimire S, Alamgeer, Akhtar MS, Adhikari A, Auger C, Schini-Kerth VB. Tambulin is a major active compound of a methanolic extract of fruits of Zanthoxylum armatum DC causing endothelium-independent relaxations in porcine coronary artery rings *via* the cyclic AMP and cyclic GMP relaxing pathways. *Phytomedicine* 2019; **53**: 163-170 [PMID: 30668395 DOI: 10.1016/j.phymed.2018.09.020]

191 **Alam F**, Saqib QNU, Ashraf M. Zanthoxylum armatum DC extracts from fruit, bark and leaf induce hypolipidemic and hypoglycemic effects in mice- in vivo and in vitro study. *BMC Complement Altern Med* 2018; **18**: 68 [PMID: 29463309 DOI: 10.1186/s12906-018-2138-4]

192 **Janbaz KH**, Qayyum A, Saqib F, Imran I, Zia-Ul-Haq M, de Feo V. Bronchodilator, vasodilator and spasmolytic activities of Cymbopogon martinii. *J Physiol Pharmacol* 2014; **65**: 859-866 [PMID: 25554990]

193 **Ghadyale V**, Takalikar S, Haldavnekar V, Arvindekar A. Effective Control of Postprandial Glucose Level through Inhibition of Intestinal Alpha Glucosidase by Cymbopogon martinii (Roxb.). *Evid Based Complement Alternat Med* 2012; **2012**: 372909 [PMID: 21792369 DOI: 10.1155/2012/372909]

194 **Aekthammarat D**, Pannangpetch P, Tangsucharit P. Moringa oleifera leaf extract induces vasorelaxation *via* endothelium-dependent hyperpolarization and calcium channel blockade in mesenteric arterial beds isolated from L-NAME hypertensive rats. *Clin Exp Hypertens* 2020; **42**: 490-501 [PMID: 31965874 DOI: 10.1080/10641963.2020.1714640]

195 **Gupta R**, Mathur M, Bajaj VK, Katariya P, Yadav S, Kamal R, Gupta RS. Evaluation of antidiabetic and antioxidant activity of Moringa oleifera in experimental diabetes. *J Diabetes* 2012; **4**: 164-171 [PMID: 22103446 DOI: 10.1111/j.1753-0407.2011.00173.x]

196 **Yu SM**, Cheng ZJ, Kuo SC. Endothelium-dependent relaxation of rat aorta by butein, a novel cyclic AMP-specific phosphodiesterase inhibitor. *Eur J Pharmacol* 1995; **280**: 69-77 [PMID: 7498256 DOI: 10.1016/0014-2999(95)00190-v]

197 **Zhao C**, Liu Y, Cong D, Zhang H, Yu J, Jiang Y, Cui X, Sun J. Screening and determination for potential α-glucosidase inhibitory constituents from Dalbergia odorifera T. Chen using ultrafiltration-LC/ESI-MS(n). *Biomed Chromatogr* 2013; **27**: 1621-1629 [PMID: 23813551 DOI: 10.1002/bmc.2970]

198 **Yin S**, Bai W, Li P, Jian X, Shan T, Tang Z, Jing X, Ping S, Li Q, Miao Z, Wang S, Ou W, Fei J, Guo T. Berberine suppresses the ectopic expression of miR-133a in endothelial cells to improve vascular dementia in diabetic rats. *Clin Exp Hypertens* 2019; **41**: 708-716 [PMID: 30472896 DOI: 10.1080/10641963.2018.1545846]

199 **Matsuura M**, Kimura Y, Nakata K, Baba K, Okuda H. Artery relaxation by chalcones isolated from the roots of Angelica keiskei. *Planta Med* 2001; **67**: 230-235 [PMID: 11345693 DOI: 10.1055/s-2001-12011]

200 **Zhang W**, Jin Q, Luo J, Wu J, Wang Z. Phytonutrient and anti-diabetic functional properties of flavonoid-rich ethanol extract from Angelica Keiskei leaves. *J Food Sci Technol* 2018; **55**: 4406-4412 [PMID: 30333636 DOI: 10.1007/s13197-018-3348-y]

201 **Lin YL**, Dai ZK, Lin RJ, Chu KS, Chen IJ, Wu JR, Wu BN. Baicalin, a flavonoid from Scutellaria baicalensis Georgi, activates large-conductance Ca2+-activated K+ channels *via* cyclic nucleotide-dependent protein kinases in mesenteric artery. *Phytomedicine* 2010; **17**: 760-770 [PMID: 20171070 DOI: 10.1016/j.phymed.2010.01.003]

202 **Yun C**, Ji X, Chen Y, Zhao Z, Gao Y, Gu L, She D, Ri I, Wang W, Wang H. Ultrasound-assisted enzymatic extraction of Scutellaria baicalensis root polysaccharide and its hypoglycemic and immunomodulatory activities. *Int J Biol Macromol* 2023; **227**: 134-145 [PMID: 36535347 DOI: 10.1016/j.ijbiomac.2022.12.115]

203 **Pires AF**, Madeira SV, Soares PM, Montenegro CM, Souza EP, Resende AC, Soares de Moura R, Assreuy AM, Criddle DN. The role of endothelium in the vasorelaxant effects of the essential oil of Ocimum gratissimum in aorta and mesenteric vascular bed of rats. *Can J Physiol Pharmacol* 2012; **90**: 1380-1385 [PMID: 22716233 DOI: 10.1139/y2012-095]

204 **Casanova LM**, da Silva D, Sola-Penna M, Camargo LM, Celestrini Dde M, Tinoco LW, Costa SS. Identification of chicoric acid as a hypoglycemic agent from Ocimum gratissimum leaf extract in a biomonitoring in vivo study. *Fitoterapia* 2014; **93**: 132-141 [PMID: 24418658 DOI: 10.1016/j.fitote.2013.12.024]

205 **Arituluk Z**, Ozkul Kocak C, Renda G, Ekizoglu M, Ezer N. Antimicrobial activity of three Scutellaria L. species from Turkey. *J Res Pharm* 2019; **23**: 552-558 [DOI: 10.12991/jrp.2019.162]

206 **Karaman Ö**, Cebe G. Diabetes and antidiabetic plants used in Turkey. *J Fac Pharm of Ankara Univ* 2016; **40**: 47-61 [DOI: 10.1501/Eczfak_0000000588]

Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: office@baishideng.com
Help Desk: https://www.f6publishing.com/helpdesk
https://www.wjgnet.com